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A CASE OF CONGENITAL CIRRHOSIS OF THE LIVER WITH RENAL TUBULAR DEFECTS AKIN TO THOSE IN THE FANCONI SYNDROME

BY

MARGARET D. BABER

From Edgware General Hospital, Middlesex

(RECEIVED FOR PUBLICATION APRIL 12, 1956)

The excretion of abnormal quantities of amino-acids in the urine is known to occur in liver disease when the cells of this organ are unable to metabolize normally, and in certain clinical syndromes in which there is a high renal clearance of amino-acids, but it is only recently that definite patterns of amino-acid excretion have become recognized (Dent, 1952-53). Fanconi (1936) first drew attention to the presence of amino-aciduria in a syndrome occurring in children, previously described by several authors including himself, and characterized by dwarfism, vitamin D-resistant rickets, glycosuria of the renal type and excessive excretion of water and phosphate. The amino-acid pattern of the urine in this syndrome has now been shown to be constant and characteristic, but it appears that other closely allied syndromes with their own characteristic amino-acid excretion patterns may also be recognized. For this reason the following case history of a patient with some unusual clinical features and biochemical findings is placed on record.

Case Report

The patient was 9 months old when admitted to hospital on June 3, 1954, complaining of failure to gain weight for three months, abdominal distension, offensive stools and nasal discharge since the age of 3 weeks.

He was the first child of healthy, unrelated parents, a little premature but in a satisfactory condition at birth (weight 5 lb.). He was breast fed for two weeks only, then put on National dried milk. He was said at the time of admission to have been quite well until 6 months old but later, when she had another child, his mother said she realized he had never been really normal. At 3 weeks his stools became loose and offensive and his abdomen distended, but he had a good appetite and gained weight steadily till 6 months when he weighed 16 lb. 14 oz. His weight fluctuated after this and was 16 lb. 11½ oz. on admission at 9 months. He started mixed feeding at 7 months and took it well, his diet being satisfactory. He had also received adequate supplements of 'adexolin' and orange juice.

Examination showed a small, thin, ill-looking, apyrexial child (Fig. 1) with prominent eyes, a very distended abdomen and copious nasal discharge. Small glands were palpable on both sides of the neck and in the right axilla, but there was no clinical evidence of tonsillar infection. Inspection of the chest revealed splayed-out ribs but no sign of rickets. The heart and lungs were normal. The abdomen was distended and tympanitic and the liver, palpable two fingerbreadths below the costal margin, felt hard and its surface slightly irregular. The spleen was just tipped, and faecal masses were also prominent on deep palpation. A lumbar kyphosis was noted and a lateral radiograph of the spine showed wedging of the body of L.1 (Fig. 2). Radiographs of the long bones (Figs. 3 and 4) showed osteoporosis with expansion of the ends of the shafts and thinning of the cortex. A patch test was negative. His haemoglobin was 70% and the differential white cell

FIG. 1.—Appearance on admission, with size of liver indicated.

FIG. 2.—Lateral radiograph of the spine indicating wedged vertebra.

count normal. Chest films showed no evidence of lung infection, but fat balance studies, undertaken because the appearance of the stools suggested steatorrhoea, showed that the child was excreting 20% of the fat ingested, and a provisional diagnosis of fibrocystic disease of the pancreas was made in spite of the negative lung findings. This was abandoned when trypsin was demonstrated to be present in normal amount in the duodenal juice.

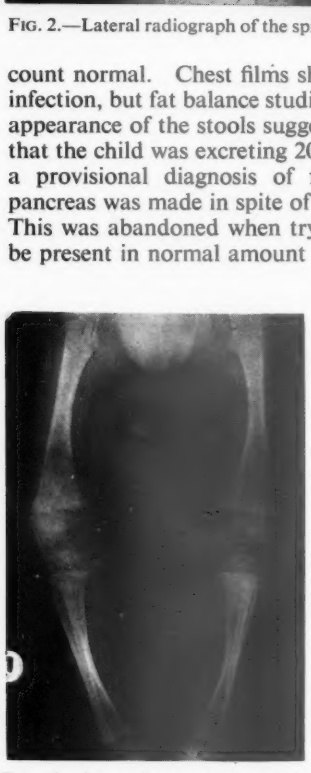

FIG. 4.—Long bones two months after admission, showing osteoporosis but no evidence of rickets.

On penicillin the nasal infection cleared and his general condition improved somewhat but the abdomen remained enlarged; he showed pink palms and soles and a primary hepatic disorder now seemed to be the main pathology. His urine showed excess urobilinogen. He was noticed to be thirsty, and to be passing excessive amounts of urine of low specific gravity which on occasion contained a reducing substance. A glucose tolerance test gave normal results, but during the test there was marked glycosuria. Liver function tests showed negative thymol turbidity, positive thymol flocculation, normal serum bilirubin and increased prothrombin time, unchanged after vitamin K had been given. A galactose tolerance test gave normal results. The serum alkaline phosphatase was 79 K.-A. units on June 4.

FIG. 3.—Radiograph of long bones (right arm) shortly after admission.

His urine was now tested for amino-acids by paper chromatography and a gross amino-aciduria of unusual pattern was found. The chromatogram pattern was not that typical of the Fanconi syndrome but was nearer to it than to any other recognized pattern. Of special interest was the relatively high excretion of tyrosine, serine, threonine, tryptophane, histidine, and lysine without increased cystine excretion.

No cystine deposits were seen in the ocular media, including the cornea, on slit-lamp microscopic examination.

The urine was constantly acid, *p*H 5·4, and blood chemistry on June 30 showed:

	mg. per 100 ml.	mEq. per litre	K.-A. Units	g. per 100 ml.
Calcium	10·6			
Phosphate	2			
Alkaline phosphatase			72	
Potassium		4·7		
Sodium		140		
Chlorides		111		
Bicarbonate		17·2		
Cholesterol	130			
Urea	22			
Sugar (resting) ..	81			
Total proteins ..				5·5
Albumin ..				4·2
Globulin ..				1·3

The electrophoretic pattern proved to be normal.

At this point the following diagnoses were considered. Amino-aciduria and mild acidosis with probable cirrhosis

of the liver suggested a variant of the de Toni-Fanconi syndrome, but the vertebral radiograph was thought to be highly suggestive, if not pathognomonic, of gargoylism or Hurler's syndrome. The enlarged liver and spleen appeared to fit in with this latter diagnosis although the child's facies were not typical. Gaucher's disease was considered, especially in view of the widening of the shafts of the long bones with cortical thinning, but a marrow puncture revealed no Gaucher cells. A diagnosis of primary hepatic disorder was also favoured especially when, as time went on, the liver became harder and somewhat smaller, and 'liver palms' became more striking. However, the amino-aciduria appeared to be mainly renal in origin, the plasma amino-nitrogen being 6·62 and 5·18 mg. per 100 ml., which is at the high range of normal. Much higher levels are generally found in cases of liver disease associated with amino-aciduria, but it is possible that the plasma level was slightly raised as a result of cirrhosis, and that this contributed to a small extent to the amino-aciduria. Other evidence of renal tubular dysfunction, i.e., glycosuria, polyuria and loss of phosphate and potassium, when taken in conjunction with the amino-aciduria, made a diagnosis of the Fanconi syndrome, or a variant of this syndrome, beyond doubt, with the addition of cirrhosis of the liver a near certainty.

Dr. C. E. Dent, who was consulted about this patient as soon as it became evident that he had a marked amino-aciduria, has very kindly supplied the following report.

FIG. 5.—Amino-acid chromatogram.

Repeated specimens of urine from the patient were analysed on two-way paper chromatograms using standard procedures and obtained from the patient during the time covering his first admission to hospital until his death. All these specimens showed a gross amino-aciduria in confirmation of the original findings of Miss E. W. M. Johnson. Whereas the spots on the amino-acid chromatogram (Fig. 5) showed a generalized excretion of amino-acids, the pattern was not the same as usually occurs in a case of Lignac-Fanconi disease (cystinosis). The especial characteristics of the pattern were that it contained relatively large quantities of tyrosine, serine, threonine and histidine. There were also excessive quantities of tryptophane and methionine.

Treatment and Progress. An attempt was made to correct the slight acidosis and tendency to low serum potassium (lowest estimation 3·9 mEq./litre) by giving sodium and potassium bicarbonate up to a total of 9 g. per day, without any effect, and this therapy was abandoned after one month. 'Calciferol', 1 mg. daily (40,000 units), was also given for three weeks from the middle of August but serum inorganic phosphate remained low and alkaline phosphatase high, and this treatment also was discontinued. The child gained 1½ lb. in weight slowly and intermittently during the four months he was in hospital, although his urinary output and degree of glycosuria increased, and he was finally discharged on October 3, to be observed further in the Out-patient Department. His treatment at this time consisted of iron medication, as he had developed a moderate degree of anaemia (Hb 64%, colour index 0·86), and ordinary vitamin supplements.

In November he was given 'calciferol', 2 mg. (80,000 units) daily, as the radiographs of the long bones still showed evidence of osteoporosis and suggested early rickets; also he continued to have a high serum alkaline phosphatase (80 K.-A. units) and low serum inorganic phosphate (1·7 mg./100 ml.). The dose was increased to 3 mg. daily in January, 1955, and eventually to 4 mg. daily in May, without any change in blood chemistry. Radiographs now showed severe osteoporosis and definite evidence of early rickets (Fig. 6). His weight fluctuated and he was more thirsty than before, his fluid intake being so great as to interfere with his eating when he was on this high dose of 'calciferol', but he tolerated 2½ mg. (100,000 units) daily quite well. In July, saucerization of the radial and ulnar epiphyses was very obvious radiologically and there was delay in formation of ossific centres. Craniotabes became apparent clinically at this time (Fig. 7), and the costochondral junctions were also enlarged. In August he showed numerous greenstick

FIG. 6.—Later film of right arm showing evidence of early rickets.

FIG. 7.—Radiograph of the skull showing craniotabes.

fractures of both forearms and now had extensive rachitic changes at the epiphyseal lines (Fig. 8).

In September he appeared to share in an epidemic of diarrhoea affecting several other members of the family and was readmitted with a history of frequent, watery, offensive stools for about one week. He was very dehydrated and his deformed chest, rickety rosary and large, hard, irregular liver were very striking. Serum sodium was 143 mEq./l. and calcium was raised to 16·8 and serum potassium reduced to 2·3 mg. per 100 ml. The blood urea level was 27 mg. per 100 ml. In spite of antibiotics, blood transfusion and electrolyte infusions, he failed to rally and died on September 24, 1955.

Necropsy. A necropsy was performed by Dr. J. L. Hamilton-Paterson 14 hours after death. The body was that of a marasmic child, extremely small for 2¼ years of age, the abdomen was protuberant, and there were multiple bony deformities.

The bones of the skull were extremely thin, especially the parietal bones which were approximately 1 mm. in thickness, and parchment-like in consistency. The pituitary fossa appeared to be greatly reduced in size and distorted, due to a grossly thickened posterior wall of the pituitary fossa, the bone of which was spongy and soft. The cerebral vessels were normal, the brain was macroscopically normal and the pituitary appeared to be intact and possibly smaller than normal.

The pericardial cavity contained a small amount of straw-coloured fluid. The heart was of normal size, and there were no congenital abnormalities; the right ventricle was distended with blood, and the wall of the left ventricle was perhaps a little thicker than normal. The valves and great vessels were normal in appearance.

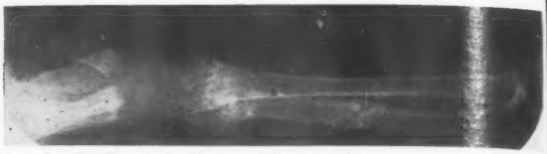

FIG. 8.—Radiograph of the right arm in August, 1955, showing saucerization of radial epiphyses and greenstick fracture of ulna.

The pleural cavities were normal. Both lungs showed congestion and oedema at the bases, but were otherwise normal. The trachea, larynx and bronchi were normal. The mediastinal glands were not enlarged.

The liver was grossly distorted by cirrhotic scarring (Fig. 9). Examination of the external surface suggested that there was little normal liver tissue. The gall bladder, ducts and pancreas appeared normal.

The spleen was moderately enlarged. Its external surface was smooth and normal in appearance, the cut surface firm and congested.

Both kidneys were grossly enlarged, and the foetal lobulation was still evident, but the cut surface showed no obvious disturbance of the normal pattern. There were some pale areas in the cortical tissue in places, and the pelvis of the right kidney was hydronephrotic but the ureter was of normal size. The left pelvis and ureter were normal, and the rest of the urogenital system appeared normal in structure. The bladder was distended with cloudy urine.

The pituitary gland weighed 133 mg. The thyroid gland appeared normal. The thymus was present but was not large for the age of the child. Both suprarenals appeared normal, and four parathyroids were found, which together weighed 55 mg.

The tongue, pharynx and oesophagus and stomach were normal. The rest of the alimentary canal showed the appearances of paralytic ileus.

The costochondral junctions showed 'rickety-rosary'. Many of the long bones showed deformities in the region of the epiphyses, and this was especially marked at the left wrist. Palpation of the bodies of the vertebrae

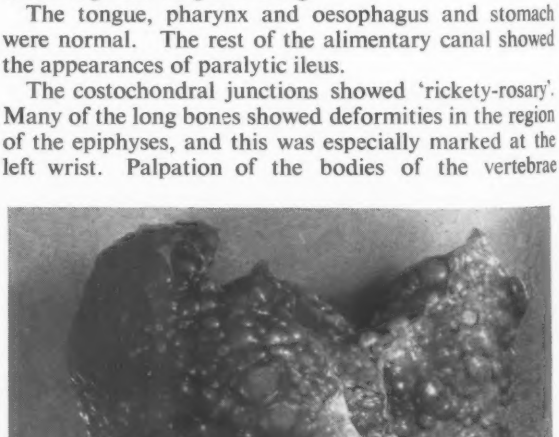

FIG. 9.—Photograph of the liver showing cirrhotic scarring.

revealed bony abnormalities of several of the lumbar vertebrae.

Histology. The heart was normal and the lungs showed hypostatic congestion only.

The liver showed gross multilobular portal cirrhosis. Mature fibrous tissue was associated with considerable bile duct proliferation and some cellular infiltration suggesting activity. There was evidence of regenerative changes. The most striking abnormality of the hepatic cells was widespread fatty change, in places very well developed; in some areas there were clear signs of adipose transformation and hepatic cell death.

The spleen showed well developed peri-sinusoidal fibrosis and congestion, presumably due to portal hypertension. There was no evidence of cystine deposition.

Pelvic fibrosis of the kidney due to hydronephrosis was seen but remarkably little parenchymal change and only one calcified tubule.

The pancreas, thyroid and three parathyroids were normal, and in the latter no hyperplasia. One piece of thyroid tissue was found. No obvious abnormality was seen in the pituitary.

The aorta was normal.

The tonsil was an active gland with mild acute and chronic inflammatory changes.

A lymph node appeared normal.

In the ribs there was irregularity and thickening of the epiphyseal cartilage. At the epiphyseal line there was irregular calcification and much newly-formed osteoid tissue and 'woven' bone. Some osteoid tissue was also present along the shaft of the bone. These bony changes were those of rickets. The marrow was cellular and appeared normal.

In the alcohol-fixed lung, spleen, gland and liver, no cystine crystals or deposits were seen.

Discussion

Cirrhosis of the liver is not an invariable feature of the Fanconi syndrome, although fatty infiltration and focal necrosis are common (Stowers and Dent, 1947). Bickel *et al.* (1952) attributed the liver changes to cystine storage, but it is noteworthy that there was no evidence of abnormal cystine metabolism in this case. Methionine was lost in excessive amounts in the urine and the liver changes could have been due to this cause, but on the other hand steatorrhoea was apparently present from the age of 3 weeks and was presumably due to hepatic dysfunction, suggesting that cirrhosis of the liver was congenital in origin.

It might be argued that osteoporosis resulted from increased faecal excretion of calcium associated with fat in the stools, but a three-day calcium balance study undertaken in September, 1954, indicated that this was not the case. In the absence of a metabolism bed and other facilities for accurate study, the figures obtained are not worth quoting, but the amount of calcium lost in the urine of this child was far in excess of that lost in the stools, whereas the normal child loses in the urine one-fifth to one-quarter of the amount of calcium excreted in the faeces. This estimation was made before 'calciferol' therapy (which may increase the excretion of calcium by the kidneys) was begun. No attempt was made to carry out a phosphorus balance, the assumption being that hypophosphataemia was similarly due to increased excretion in the urine.

Rickets developed in this patient while he was taking large doses of 'calciferol', and he appeared to be wholly resistant to the vitamin. The serum alkaline phosphatase level remained high in spite of the treatment and was obviously uninfluenced by it. The serum phosphate never exceeded 2·3 mg. per 100 ml., and this fact suggests that vitamin D therapy did not result in increased absorption of phosphorus from the intestine, which is at variance with the experience of Bickel *et al.* (1952).

No other case of metabolic disturbances has occurred in this family at any time. The patient's younger sister was healthy and well grown at 1 year old, and her urine was normal.

Summary

An infant suffering from gross amino-aciduria of a distinctive type, with other manifestations similar to those found in the Fanconi syndrome, is described.

Cirrhosis of the liver in an advanced stage was present when the child was first seen at the age of 9 months, and the history suggests that it was congenital in origin.

Rickets developed and progressed in spite of the administration of large doses of 'calciferol'.

The nature of the metabolic disturbance is discussed very briefly.

I am very much indebted to Dr. C. E. Dent for help and advice in the investigation and treatment of this patient, and for criticism and suggestions. I also wish to thank Miss E. W. M. Johnson for the initial chromatogram and other biochemical investigations, Dr. J. L. Hamilton-Paterson for the necropsy report, Dr. R. A. B. Drury for the histological findings and Mr. H. H. Skeoch for his examination of the ocular media.

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ESCHERICHIA COLI GASTRO-ENTERITIS

BY

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(RECEIVED FOR PUBLICATION APRIL 25, 1956)

PART I

The Incidence of Pathogenic *E. Coli* in Normal Babies in the General Community

Mild gastro-intestinal upset is common in babies, but severe disease is not now the scourge it formerly was, and part of the great improvement in infantile mortality is due to its decline in the twentieth century. The reasons for this are not clear, and many theories have been advanced. Formerly, a considerable number of cases of gastro-enteritis were thought to be due to dietetic, that is to say chemical upsets, but it is now believed that infection is the responsible factor for almost all cases. It has been known for a long time that dysentery bacilli and salmonellae cause only a small proportion of the cases, and many other bacteria have been suspected from time to time. One theory dating back to the early years of this century is that the disease is caused by the invasion of the small gut by the flora of the large gut (Moro, 1916). Adam (1922, 1923, 1927) advanced the view that there were certain varieties of *Escherichia coli* associated with the disease and based his classification upon biochemical tests. Goldschmidt (1933) showed that the strains of *E. coli* described by Adam fell into a few serological groups.

The significance of this earlier work was not at first fully appreciated when certain O groups of *E. coli*, classified according to the Kauffmann scheme, were shown to have an association with gastro-enteritis in babies. The first of these, *E. coli* O111, was described by Bray in 1945, and soon afterwards O55, O26 and O119 were described by Giles and Sangster (1948), by Smith (1949, 1953), and by Taylor and Charter (1952). The evidence incriminating these O groups was until recently epidemiological, but Thomson (1955a) showed that the whole length of the gut is colonized in the disease. The syndrome of gastro-enteritis has thus striking similarities to the syndrome of cholera: the whole length of the gut and often the gall bladder swarm with the pathogen; there is no acute inflammation of the gut in the pathological sense; there is vomiting as well as diarrhoea, and collapse occurs because of fluid loss and electrolyte imbalance. The old name 'cholera infantum' would appear to be a very fitting one.

With few exceptions, most of the literature on gastro-enteritis associated with *E. coli* deals with hospital outbreaks, many of which have been very troublesome because infection, once introduced, may linger for a long time (Rogers, 1951; Rogers and Koegler, 1951; Wright and Roden, 1953; Jameson, Mann and Rothfield, 1954). In most areas where a study has been made of the disease the majority of cases yielding the suspected varieties of *E. coli* have arisen from cross-infection in hospitals. For example, in the Cardiff area in 1953, the year before the surveys described in this publication, 80% of the recognized cases had such an association as the following table shows.

SOURCE OF STRAINS OF *E. COLI* IN 1953

Source	Type of Organism			Total
	O55	O111	O26	
Hospitals and institutions	80	16	13	109
Other sources	21	1	6	28
Totals	101	17	19	137

Mild forms of gastro-enteritis are common in the first year of life, but the proportion of these cases caused by *E. coli* is not known as the general practitioner may not be summoned, and if summoned may not think the case serious enough to warrant laboratory investigations. There is, therefore, a suspicion that many mild cases of 'coli-enteritis' exist outside hospitals. To determine this and the number of symptomless excreters a special investigation was made of babies attending a Cardiff City infant welfare clinic.

Scope of the Survey. Babies attending one of the Cardiff City's public health infant welfare clinics were enrolled in the survey. Babies are normally

brought to the clinic when they are 4 to 6 weeks old and thus the neonatal period was unexplored. In all, 111 babies were investigated and the ages at which they first attended were: first month, 3; second month, 56; third month, 26; fourth month, 13; fifth month, 4; sixth month, 5; seventh month, 2; eighth month, 1; ninth month, 1. Most of the babies (77%) were in the survey before they were 3 months old.

Mothers were asked to send to the laboratory a specimen of faeces from their babies at fortnightly intervals. A swab was sent to the mother a few days before the next specimen was due, and on the whole the mothers cooperated well. The general practitioners of the district were informed of the investigation but not asked to take part.

The fundamental aim was to determine how many babies became infected in the first year of life, and how many developed symptoms of gastro-enteritis. The babies were not kept in the survey after they were 1 year old. The specimens were examined for *E. coli* O111, O55 and O26.

In cases of hospital gastro-enteritis it has been observed that practically the whole coliform content of the faeces consists of the suspected pathogen. This might not occur in symptomless excreters, and if the special O groups of *E. coli* are outnumbered 100 : 1 by other *E. coli* it would be necessary to pick and examine, on the average, 100 colonies before a positive result would be obtained (Thomson, 1955b). Thus many positives are missed, and until a selective culture medium can be found this problem will remain. The effect of this in a survey of the kind reported here must be that the number of excreters identified is a considerable under-estimate.

Results. In all, 1,681 specimens of faeces were examined from 111 babies, and 20 babies (18%) were found positive at one time or another. The following strains of *E. coli* were identified.

O26 B6 H11, 9 strains; O26 B6 H?, 3 strains;
O55 B5 H21, 2 strains; O55 B5 H7, 4 strains;
O55 B5 H27, 1 strain; O111 B4 H?, 1 strain.

The strains were identified by agglutination of their O, B and H suspensions to the full titre of antisera. At least five different varieties were identified and this might be advanced as evidence that the babies were not picking up the infection when visiting the clinic.

In nearly all positive cases a repeat specimen was taken the following day to confirm the result, but in only one case was the specimen still positive at the next routine fortnightly examination. The rate of clearance, or apparent rate of clearance, in these babies was rapid, and many more babies would presumably have been found positive had swabs been taken at more frequent intervals. For this reason, and for the technical reasons given above, the incidence of 18% is almost certainly a considerable underestimate of the proportion of babies infected by the special O groups of *E. coli* in the first year of life. The figure of 18% might be shown as 25% per annum as the babies, on the average, were investigated for only nine months of the first year of life. In all, 1,681 specimens of faeces were examined and 21 found positive, a result which indicates that just over 1% of babies under 1 year are, at any one time, harbouring the strains of *E. coli* associated with gastro-enteritis.

The numbers were small in which to ascertain any relationship with the type of feeding, but the following analysis is given:

Number of specimens from babies receiving only breast milk (none positive)	121
Number of specimens from babies receiving breast milk and other foods (two positive)	208
Number of specimens from babies receiving no breast milk (19 positive)	1,352

No new evidence was found of the value of breast milk, but a more extensive survey of this kind might show what part, if any, is played by breast milk in protecting a baby. The immunity of the breast-fed baby may not depend upon any special immunological quality of the milk, but upon a decreased exposure to exogenous infection conveyed by other foodstuffs.

How the babies become infected is not clear. In a recent study Thomson (1956) found 1% of samples of cow's milk to be contaminated by these same O groups of *E. coli*, but none of the babies in the survey drank unheated cow's milk and only one household bought unpasteurized milk. Many babies were fed on dried milk, but this is heated before drying and is expected to be free from coliforms. Much more work will be necessary to find out how babies in their own homes become infected, and unfortunately the lack of a selective culture medium will make this a very difficult if not impossible task. The problem is to isolate the special O groups when they are present only in small numbers.

It was thought of value to ascertain if the infected babies acquired their infection shortly after the introduction of mixed feeding, including cow's milk, or if the risk remained more or less uniform throughout the first year of life. The interval elapsing between the cessation of full breast-feeding and infection was 0-1 month in 2 cases, 1-2 months in 2 cases, 2-3 months in 5 cases, 3-4 months in 1 case, 4-5 months in 2 cases, 5-6 months in 2 cases, more than 6 months, 6 cases. Having regard to the fact that examinations were made only once a fortnight,

the term 'month' as used above has no accurate meaning, but the simple analysis suggests that a baby may have a greater tendency to become infected shortly after the introduction of other foods, including cow's milk, into the diet.

There was a tendency for more positives to be identified in the summer. Of the 20 babies found positive, 14 were identified in the months April to September (818 specimens examined) and the other six from October to March (863 specimens examined).

Only eight of the 20 identified excreters had loose stools and only one baby, infected with O55 B5 H21, was sufficiently ill for the general practitioner to be called. This baby was admitted to hospital (what may happen when an infected baby is sent to hospital is described in Part II of the report). All the other babies had recovered within three days, the majority having symptoms for only 24 hours.

Another 29 babies had mild diarrhoea at one time or another, but yielded no identifiable strains of *E. coli*. Thus, from a little more than one-fifth of all cases of diarrhoea identifiable strains were isolated, but as the examinations were restricted to O groups 111, 55 and 26, leaving out 119, 128, etc., it is possible that an appreciably greater proportion might have been found positive had the bacteriological examinations been more comprehensive.

On 17 occasions it was possible to obtain specimens of faeces from other members of the family when the baby was found positive. Five family contacts were found to be excreting the same organism as the baby, and on three of these occasions it was the mother who was positive.

Discussion. In this survey of babies in the first year of life the infection rate by the special O groups of *E. coli* associated with gastro-enteritis was 25% per annum. Having regard to the technical difficulties and to the fact that specimens of faeces were examined at only fortnightly intervals, the suspicion arises that most, if not all, babies are infected in the first year of life. Most of the infected babies were not ill, approximately one half having symptoms, and only one baby was ill enough to warrant admission to hospital.

Many different varieties of *E. coli* were encountered in the survey, but all had previously been isolated in the Cardiff area. Nine babies were infected with O26 B6 H11, and though this serotype is a very common one in Cardiff and district it has not been responsible for outbreaks of severe disease. Most of the earlier strains had been isolated from mild cases and symptomless excreters in residential institutions. Four babies in the survey were infected with O55 B5 H7, a serotype which had been previously isolated only from symptomless excreters in residential institutions. One baby was infected with 055 B5 H27, and the only strain of this serotype previously encountered in Cardiff was isolated from a chicken (Thomson, 1956). Two babies in the survey were infected with O55 B5 H21 and one of these babies was ill enough to warrant admission to hospital; this serotype had been isolated before from only two babies both of whom died.

It would appear that there might be great differences in virulence from strain to strain possibly within any O group. There may be a correlation between H antigen structure and virulence, but it is also possible that there are minor differences in the O antigens within an O group.

Babies at home are commonly infected by strains of *E. coli* associated with gastro-enteritis. The sick baby, infected by one of the more virulent varieties, is the one which is sent to hospital. What may happen after infection is carried into hospital in this way is described in Part II of this report.

PART II

The Spread of *E. Coli* Infection in Hospitals and Institutions

Gastro-enteritis is highly infectious among babies in hospital, and barrier nursing of a quality expected to prevent the spread of other intestinal diseases is commonly inadequate. How the infection spreads within institutions is not fully known.

Many hospital outbreaks of severe infantile gastro-enteritis associated with certain O groups of *E. coli* have been recorded in recent years. On the other hand it has happened not infrequently that infection by some of these O groups has spread in an institution and not caused an outbreak of serious disease. It would seem that some varieties, as in the case of the salmonellae, are much more virulent than others.

In Part I of this report evidence was advanced that many babies living at home are infected by these O groups of *E. coli* in the first year of life. One hundred and eleven babies were repeatedly examined during the first year of life and 20 of them were found to be infected at one time or another. Only one of the babies, infected with O55 B5 H21, was ill enough to be sent to hospital and it may be that our hospitals, by a process of selection, are breeding centres for the more virulent varieties. Many hospital outbreaks have lasted for a long time, since infection, once introduced, is not easily removed.

This paper reports an extensive outbreak of severe gastro-enteritis in a group of widely separated

hospitals in South Wales. Within each hospital the events followed the classical pattern frequently described in the literature in recent years and are therefore presented briefly in order that emphasis can be laid on the special evidence yielded by the South Wales epidemic, viz., the carriage of infection from one hospital to another by the transference of infected babies. The strain of *E. coli* responsible for the epidemic had the antigenic structure O55 B5 H2, and as it had a definite 'antibiotic sensitivity' pattern it could be identified with precision and followed from place to place.

Events before the Epidemic of 1954. Strains of *E. coli* associated with gastro-enteritis have been identified for some years in Cardiff. The bacteriological supervision of the disease is particularly close over the wards of the University Department of Child Health in Llandough Hospital, Cardiff. Following an outbreak in the babies' ward in 1953 a large side-ward with six cots has been set aside for cases in order to minimize the risk of spread of infection. This side-ward is part of the unit for older children and on another floor from the babies' ward proper. In addition, all babies are examined on admission to detect carriers and at weekly intervals thereafter to detect any spread of infection.

Early in 1953 there was an outbreak of gastro-enteritis in Llandough Hospital and another in Church Village Hospital which lies 10 miles north of Cardiff. The outbreaks were caused by *E. coli* O55 B5 and the limited number of strains which were examined more fully were shown to have H antigen 2. The few strains which had been preserved were shown to be sensitive to chloramphenicol, partly sensitive to terramycin and resistant to sulphonamides, streptomycin and aureomycin. The epidemic in 1954 reported here was caused by an identical organism.

The 1953 outbreaks ended in the early summer, and in Llandough Hospital where the babies' faeces were regularly examined, the epidemic strain of O55 B5 H2 was not once encountered from September to December. During these four months, in spite of weekly examinations of specimens from all babies, only two strains of O55 were isolated and both had H antigen 6.

The Outbreaks of 1954

Church Village Hospital. This hospital has 40 children's beds and cots, and on an average has 10 babies under 1 year old at any one time. Routine bacteriological examinations for the special varieties of *E. coli* were not made on all babies admitted, but cases of enteritis were so examined. Within the limits of these clinical and bacteriological criteria the department had been free of gastro-enteritis for nearly a year, i.e., since the outbreak referred to above.

Towards the end of January, 1954, a number of babies developed gastro-enteritis; the infecting strain of *E. coli* had the antigenic pattern O55 B5 H2 and had the antibiotic sensitivities given above. The usual precautions were taken to prevent the spread of infection within the hospital and the infected wards were closed to new admissions. The infection lingered in the wards for 11 weeks; in all, 23 babies were infected, many were seriously ill and one died.

Unfortunately, in the few days before the outbreak began, and when some of the babies were presumably incubating the disease, a number were discharged and apparently carried the infection with them. These babies were responsible, in one way or another, for introducing infection into a number of institutions where outbreaks followed. The events are best described by following the babies. The three babies concerned named Susan M., aged 7 months, Philip P., aged 4 months and Howard M., aged 4 months, were discharged from Church Village Hospital at the end of January, 1954.

Baby Susan M., and Residential Nursery. Baby Susan M. had no home and lived in a residential nursery five miles away. When she had severe bronchitis she was admitted to Church Village Hospital for treatment and was returned cured to the residential nursery on January 27, 1954, i.e., on the day before cases of gastro-enteritis appeared in Church Village Hospital. Baby Susan M. remained well, but another baby (Brian E.) in the residential nursery fell ill with symptoms of gastro-enteritis so severe that he was sent to the special unit in Llandough Hospital, Cardiff. Bacteriological examinations showed both Baby Susan M. and Brian E. as well as eight other infants in the nursery to be infected with *E. coli* O55 B5 H2 possessing the antibiotic sensitivities given above. Presumably Baby Susan M. had carried the infection from Church Village Hospital to the residential nursery.

Baby Philip P., and Paediatric Unit. Baby Philip P. was also discharged from Church Village Hospital on January 27, 1954, and he went to a small paediatric unit eight miles away. Two weeks later two babies in this small hospital fell ill with gastro-enteritis and the epidemic strain of *E. coli* O55 B5 H2 was isolated. An examination of the other 15 children in the hospital revealed five more to be symptomless excreters.

Baby Philip P. had meanwhile gone home (he

went home four days before the outbreak began in the small paediatric hospital), but he was followed up and he too was found to be excreting the epidemic strain. It was thought reasonable to conclude that he had brought the infection from Church Village Hospital to the small paediatric hospital.

Baby Howard M., and Llandough Hospital. Baby Howard M. was discharged from Church Village Hospital at the end of January, 1954. A few days later he fell ill at home with vomiting and diarrhoea, and he was sent direct to the special gastro-enteritis unit at Llandough Hospital, Cardiff. This hospital thus admitted two babies both infected by the epidemic strain, viz., Baby Howard M. who had gone from Church Village to his own home and Baby Brian E. who came from the residential nursery to which infection had been carried by Baby Susan M.

In spite of the isolation afforded by the special side-ward, and the fact that the staff are constantly alert to the risks of cross-infection, there was an outbreak of gastro-enteritis within the department. The infection spread to the babies' ward on another floor of the hospital in spite of the fact that they were nursed in isolation cubicles. The infection lingered for 10 weeks. In all, 22 babies were infected, many were very ill and five died.

Thus if the outbreak in Church Village Hospital is regarded as the first generation, the outbreaks in Llandough Hospital, the residential nursery and the small paediatric hospital were second generation. Unfortunately, there were third generation outbreaks in two fever hospitals which were prevailed upon to help the other institutions to cope with their problem.

First Isolation Hospital. The problem had arisen of how to dispose of infected babies and toddlers in the residential nursery. Eventually there remained only six infected but symptomless toddlers aged 2-3 years, and in order to allow the nursery to re-open they were sent to a large isolation hospital. They were accommodated in the largest room of a cubicle block which had 10 rooms opening on to a large veranda, and the room with the infected toddlers was at one extreme end of the veranda.

In spite of the ideal conditions, and the fact that the children had no diarrhoea, and the staff were trained fever hospital nurses, infection spread within the unit. At the extreme other end of the cubicle ward were several babies suffering from whooping cough, and two weeks after the toddlers had been admitted for isolation one of these babies developed gastro-enteritis. Thereafter, the infection remained in the ward for 12 weeks spreading from baby to baby, all of whom were infected by the epidemic strain. There were in all eight cases; some were very ill and one died.

Second Isolation Hospital. None of the babies who remained in the small paediatric unit was very ill, and in time most became free of infection as judged by bacteriological tests. At length only two babies remained infected, and in order that the small paediatric unit might re-open, these two babies were sent to an isolation hospital nearby.

This isolation hospital has a special wing of five rooms each holding one bed or two cots. These rooms were in a suite and each had a separate door. In spite of these conditions two other babies already in the ward became infected with *E. coli* O55 B5 H2 with the antibiotic stamp of the epidemic strain, one baby being infected two weeks and the other six weeks after these babies had been admitted for isolation.

Other Hospitals. All the hospitals and institutions mentioned in this report are in the county of Glamorgan, but it was known that there were extensions into hospitals in the neighbouring county of Monmouth. No serious attempt was made, however, to follow the trails into the next county where there were many cases with at least three deaths.

Part Played by Adult Carriers

To the problem of how infection spreads within an institution this report makes no contribution. When gastro-enteritis spreads in a babies' ward it is customary to suspect the adult staff of playing a part in spreading it, either by failing to observe the techniques to prevent cross infection or by acting as carriers of the infection. When children suffer from salmonella food-poisoning or dysentery, carriers are not infrequently found among the adult staff. In studies of outbreaks of gastro-enteritis nurses and other adult attendants can rarely be shown to be infected. It has been pointed out that the difficulty of finding small numbers of these special varieties of *E. coli* when outnumbered by other *E. coli* in faeces is a great one, and many excreters may thus fail to be identified.

In the outbreaks reported here, bacteriological examinations were made of nurses, doctors and other attendants. In Llandough Hospital, 19 were examined and none found positive; in the small paediatric hospital, 16 were examined and none found positive. In Church Village Hospital, 44 were examined and one male nurse was found to be excreting *E. coli* 055 B5 H2. This was the antigen

structure of the epidemic strain but the sugar fermentation reactions and the sensitivities to antibiotics differed from those of the epidemic strain. In the residential nursery 19 adults were examined and one found to be excreting the epidemic strain of *E. coli* O55 B5 H2. Four, however, were found to be excreting *E. coli* O111 B4 H6. Three weeks previously six members of the staff, including the four harbouring *E. coli* 0111 B4 H6 at the time of examination, had suffered from diarrhoea, and it was difficult to avoid the conclusion that *E. coli* O111 B4 H6 was connected with this incident. *E. coli* O111 B4 H6 was isolated also from three babies in the nursery.

When Baby Philip P. was examined in his own home and found to be excreting the epidemic strain *E. coli* O55 B5 H2 (he was the baby suspected of having carried the infection from Church Village Hospital to the small paediatric unit) it was decided to examine his family. No member of the family was found to be excreting O55 B5 H2, but the father was excreting *E. coli* O111 B4.

Thus it happened that seven adult contacts were found to be harbouring pathogenic varieties of *E. coli*, but only one was excreting the epidemic strain.

If there is a moral to this investigation it is to stress the danger of admitting small babies to hospital direct from another institution and that there is much less risk of a baby contracting infection at home than in hospital.

Summary and Conclusions (Parts I and II)

Pathogenic varieties of *E. coli* were found in 1% of faecal specimens from babies under 1 year old living at home. The infection rate was shown to be at least 25% per annum.

Outbreaks of *E. coli* gastro-enteritis caused by *E. coli* O55 B5 H2 were traced through six hospitals in South Wales. Transference of infection from one hospital to another was shown to be via infected babies.

Infection by pathogenic strains of *E. coli* is common among babies living at home, but there would appear to be a great variation in virulence from variety to variety and our hospitals, by a process of selection, are breeding the more virulent ones. The breeding in hospitals of strains of bacteria of enhanced virulence is not a new observation, but *E. coli* gastro-enteritis presents yet another example.

We wish to express our thanks to Miss A. Davey, health visitor to the Cardiff Public Health Department, for visiting homes to collect information of value to the survey. Our thanks are also due to Mrs. Steed for her record keeping, and to John Smith for his technical help.

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OSTEOGENESIS IMPERFECTA

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Osteogenesis imperfecta is a disease of infancy and childhood, but it has been observed in all age groups. It is characterized by increased fragility of the bones, which fracture on minor trauma, resulting in severe or lesser degrees of crippling. The eyes may be prominent and the sclerotics blue. The neck is usually short, the thorax misshapen, the vertebral column angulated, and the limbs bent.

In the severe form of the disease fracture deformities may occur *in utero* or the bones may break during parturition. Many of these cases of osteogenesis imperfecta congenitalis are stillborn or succumb shortly after birth.

In the less severe form, osteogenesis imperfecta tarda, the baby is apparently normal at birth, and only after the lapse of several years are multiple fractures encountered; this tendency to fracture disappears at puberty. Fairbank (1951) describes a case of a young girl with striking blue sclerotics who sustained the first of many fractures at the age of 7.

Most patients die young, but a few survive for many years despite the severity of the disorder. Fairbank notes two cases. One, a boy, a prenatal case, was alive at the age of 19, though bedridden since birth. The other, a girl, also a prenatal case, only slightly less severe and markedly deformed, is still able to earn a living as a secretary at the age of 29.

Lawford Knaggs (1924) cites a patient with multiple fractures at birth, who evidently earned his living even though a cripple for many years, but who in later years was poverty stricken, and as a result of hunger malacia died from multiple fractures at the ripe old age of 68.

Brailsford (1953) states that the plasticity of the bones during infancy and adolescence, which causes the pronounced curvatures and deformities, appears to consolidate in early adult life. There is little or no progress in the deformity in later life.

Aetiology and Pathology

The aetiology is unknown; there is, however, a hereditary trait. Fairbank states that hereditary and familial influences play a part in the minority of prenatal and post-natal cases, the disease being transmitted by either parent. Family trees have been recorded covering four generations but not all the individuals in the family have been equally affected. Blue sclerotics have been present in some, otosclerosis in others, while in yet others there were multiple fractures in the absence of blue sclerotics or otosclerosis. Roger (1936) states that 60% of the cases with blue sclerotics tend to develop otosclerosis.

Bickel, Ghormley and Camp (1943) reviewed 40 cases at the Mayo Clinic and reported that blue sclerotics were consistently associated with the hereditary type but not with the non-hereditary type. In their series 27·5% were hereditary and 72·5% had no known family history of the disease. They found deafness in 45·5% of the hereditary type and only 17·3% in the non-hereditary cases. The family tree may thus reveal flail joints and recurrent dislocations in one member, deafness and otosclerosis in another and blue sclerotics or cutis laxa in a third. Considered thus, this departure from the normal is attributable to mesencyhmal dysplasia hereditarily dominant.

Osteogenesis imperfecta is a systemic disease of the mesenchymal tissues of the body, thus some tissues derived from the mesenchyme (sclera, ligaments, bone supporting tissue) are inferior and exhibit the characteristic stigmata. Other mesenchymal tissues, however, appear normal.

The skin of patients suffering from osteogenesis imperfecta is thin and of a fine texture, occasionally with atrophic blotches. Bauer (1920) found a systemic defect in the development of connective tissues with a greater variety of cell forms than is normally encountered. The differences are more pronounced in the more specialized tissues.

Follis (1952) by his histiogenetic examinations corroborates this finding: reticulum spindles are not properly converted into collagen fibres. Biering and Inversen (1955) describe a case of osteogenesis imperfecta with an accompanying Ehlers-Danlos syndrome.

No hormonal deficiency has been cited as a causal factor.

On pathological examination it has been determined that the cortex is thin as a result of the impaired periosteal bone formation, diminished osteoblastic activity and diminished calcium deposition, because the collagen matrix is defective. The result is incomplete ossification, soft and fragile bones which bow and fracture. After fractures, adequate callus is formed but not replaced by strong bone so that fractures can ensue at these same sites.

The thin sclerotics allow the underlying pigment to become visible. Deafness, usually in the third decade, is a result of otosclerosis or labyrinthine disturbances.

The ligaments are lax and the muscles hypotonic. This can result in bowing and multiple fractures of the long bones and ribs, compression of vertebrae, a triradiate pelvis and temporal bulging of the skull which in some cases sags on to the cervical vertebrae like a 'tam-o'-shanter'. Thus eventually a severe dwarf-like deformity ensues.

The number of fractures encountered in individual cases is variable. Fairbank (1951) states that in severe cases the fractures are spontaneous and relatively painless. In newborn babies, as many as a hundred fractures may be present, mostly of the ribs. He describes a patient with deep blue sclerotics who died at the age of 8 years, after sustaining 98 fractures.

In one of our cases the patient was apparently perfectly normal in appearance until at the age of 4 years the vertebrae collapsed and he developed a curved spine and bent legs. Previously he could play with other children freely. Recently he injured the thorax and radiological examination revealed three fractured ribs—the left ninth, tenth and eleventh ribs; only these six fractures were encountered in the skeletal survey and they revealed union with ample callus. This case is typical of osteogenesis imperfecta tarda.

Von Lobstein (1833) was evidently the first person to describe the post-natal group under the designation of osteopsathyrosis idiopathica. Vrolik (1849) coined the term osteogenesis imperfecta to describe the ante-natal group.

In view of the fact that osteogenesis imperfecta is encountered at all ages, Brailsford (1943) recommends that terms like 'osteopsathyrosis idiopathica', 'fragilitas ossium' and 'hereditary fragility of bone' and many similar designations merely refer to various examples of the same dystrophy and should be discarded in favour of the all-embracing term of osteogenesis imperfecta. He regards Vrolik's osteogenesis imperfecta, or the ante-natal form as the most severe example, whilst the less severe types are encountered post-natally. Osteogenesis imperfecta has now been universally recognized as the most acceptable term for this dystrophy.

Classification

Osteogenesis imperfecta is the all embracing term used today to include the foetal, infantile, adolescent and adult examples of the disease. Although osteogenesis imperfecta is a general bone disease that is present from birth, the clinical and radiological features seem to differ quite prominently in the various age groups. It therefore seems feasible, for the sake of clarity, to divide osteogenesis imperfecta into four age groups, as suggested by Vernon Luck (1950), but admitting that there is no very clear cut division between these age groups.

The classification we suggest is as follows:

(1) Osteogenesis Imperfecta Congenitalis. The condition can be recognized *in utero*. These cases are usually stillborn and represent the most extreme examples of the disease, which is characterized by multiple fractures and deformities. At birth the skull is usually collapsed for it possesses little ossification and cannot stand up to the strain of parturition. Knaggs describes such a skull as a 'membranous bag of bones'.

Fairbank describes these cases as the prenatal thick bone type, and says that these are the severe cases born with limbs that are stunted as in achondroplasia and with numerous fractures, notably in the ribs. The major long bones are thick, blunt and stunted. They have a crumpled up appearance due to one or more fractures, which apparently do not perforate the periosteum and which are associated with ample callus. These typical radiological changes are seen at birth or up to three months after birth if the baby survives as long as that.

(2) Osteogenesis Imperfecta Infantis. This type represents a less severe degree of skeletal deficiency. These cases usually live from one to eight years, during which time they sustain innumerable fractures, following even the mildest trauma, from which they eventually succumb.

Fairbank describes these cases as the slender fragile bone type, and says the condition is seen in prenatal cases which survive more than a few months, and in all post-natal cases. The skeleton as a whole is osteoporotic and the long bones are soft, fragile and slender. The cortex is practically absent; the epiphyseal extremities are by contrast abnormally large, and are sometimes honeycombed. Transverse lines of dense bone, straight or wavy, often mark the ends of the metaphysis. The skull is usually extremely thin, and the petrous bones by contrast

excessively dense. The soft skull sags over the cervical spine in 'tam-o'-shanter' style. There is extreme compression of the soft and osteoporotic vertebrae which exhibit biconcave articular surfaces. The soft pelvis becomes triradiate due to compression. Deformities due to fracture or bending of the long bones are common. The ribs are especially prone to multiple fractures causing deformity of the thorax. These patients end up as miserably deformed dwarfs.

(3) Osteogenesis Imperfecta Tarda. In these cases there is usually far more substantial ossification of the skeleton at birth than in the foetal and infantile types, in fact, some of these patients pass through an uneventful infancy and early childhood before they begin their careers of multiple fractures. A delay of the first fracture until after the age of 5 years is generally recognized as representing a case of osteogenesis imperfecta tarda.

Fairbank (1935) was the first to suggest the name of osteogenesis imperfecta cystica for an exceedingly rare example of the disease. Only three cases have been recorded, all by Fairbank. During the first few years of life the limbs may show no more than osteoporosis, though the condition dates from birth. Cystic changes which are more pronounced in the lower than in the upper limbs become increasingly evident with advancing years. Deformity due to fracture and bending of bone is progressive, and with advancing years all the bones of the body, including the skull, show marked cystic changes. Fairbank had occasion to follow one of these cases from the age of 5 until she died at the age of 23. Honeycombing was distributed throughout the whole skeleton, becoming more evident with age.

Brailsford (1943) reported four cases of 'a condition suggesting scurvy, subperiosteal haemorrhages being more frequent than fractures occurring as a complication of osteogenesis imperfecta. This was followed by a paper by Baker (1946) on 'Hyperplastic Callus Simulating Sarcoma in Two Cases of Fragilitas Ossium'. Fairbank and Baker (1948) published details of eight cases of osteogenesis imperfecta that developed hyperplastic callus formation. The bones affected were one or both femora in every case, the humerus in four cases, and the radius and ulna less frequently. Both sexes are affected, and the age at which it occurs is usually from 1 to 15 years. Fairbank states that the cause of the curious features found in these cases is obscure. He says that Brailsford's suggestion of scurvy playing a part is contradicted by the fact that Baker failed to find the faintest sign of haemorrhage, old or recent, in his sections and there was strong evidence against lack of vitamin C in these cases.

(4) Osteogenesis Imperfecta Adulta. This condition, although rare, occurs and must be included to round off the classification. These cases include all cases that appear to have recovered from the condition during infancy and adolescence, only to develop skeletal fragility again in adult life. The case described by Lawford Knaggs and cited in this article is a good example of osteogenesis imperfecta adulta.

Case Reports

Case 1. John, a 5-year-old Bantu boy, is an example of osteogenesis imperfecta tarda. He was admitted to the Pretoria Hospital for investigation. During the course of the previous year his legs became gradually weaker and at present he is unable to walk and is a crippled dwarf.

His mother avers that he had been quite well at birth and had played normally with other children until a year ago. She then noticed that his back and right leg became bowed. Recently he hurt himself and complained of pain in the left side of the chest; this is slightly better now.

There were eight children in the family, two died at a tender age (probably measles in the one case and an accident in the other). The father is an epileptic and does not work. The mother is the breadwinner; she takes in washing and cares for the children.

The other five children are well and normal. John had measles as a baby and was vaccinated against smallpox. There were no maternal pre-natal complications, and his birth was normal. He was breast fed for three years and mealie porridge subsequently formed his main diet.

On examination he was an obvious crippled dwarf as the photograph illustrates (Fig. 1). He has blue sclerotics. He is poorly nourished. There are no tender areas. The skin covering the elbows is loosely attached, thickened and hyperpigmented. Most of the long bones are bowed to a variable extent. The head has descended on to the neck creating the impression of a short thick neck. There is a striking kyphosis of the thoraco-lumbar area with a barrel-shaped chest and atrophy of the trunk muscles. There is also atrophy of the limb muscles, especially of the lower extremities. The joints appear normal and there is no abnormality of the heart, lungs, or abdomen.

A blood Kolmer test was negative and the sedimentation rate normal.

A blood count gave: Haemoglobin 10·3 g. per 100 ml. (71%); R.B.C.s, 4,290,000, W.B.C.s, 6,000 (polymorphs 45%, lymphocytes 50%, monocytes 4%, eosinophils 1%). Platelets were normal. The blood calcium level was 10·2 mg. %, phosphorus 3·8 mg. %, alkaline phosphatase 15·5 K.-A. units. Urine was negative for albumin and no red or white cells were seen. The glycien, alanine and methyl histidine excretion was normal.

RADIOLOGICAL SIGNS. The following were of importance:

FIG. 1.—Bantu boy age 5.

Skull. The skull is thinner than average (Fig. 2), the parietal areas bulge laterally and the base is definitely descended on to the upper cervical vertebrae (Fig. 3). The petrous bone is elevated on the left side. The sutures, fontanelles and sella turcica are within normal limits. The facial bones are small in relation to the vault.

Spine. There is a kypho-scoliosis of the upper spine (dorsal and proximal lumbar vertebrae) with obvious general osteoporosis and flattened deformity of all the vertebrae in the thoraco-lumbal vertebral column; wedge-shaped vertebrae especially, (Fig. 4), as well as a few biconcave and symmetrically flattened vertebral bodies (vertebra plana), are present.

Pelvis. Gross asymmetry and distortion, with the formation of a triadiate pelvis, are present with definite osteoporosis (Fig. 5).

Thorax. There is a slight degree of distortion and asymmetry with rib fractures exhibiting marked callus formation (Fig. 6). There are fractures of the right second and ninth ribs (anteriorly) and the seventh rib (posteriorly) as well as the left ninth, tenth and eleventh ribs (posteriorly).

Long Bones. Generalized osteoporosis with thin cortex and poor trabeculae is seen. The femora, tibiae and humeri are thinner than normal while the fore-arm bones are considered to be within normal limits.

The right femur is acutely curved anteriorly and the left tibia and fibula so to a lesser degree.

FIG. 2.—Pencil outline of skull.

Looser zones are observed in the proximal humeral shafts, right femur, proximal left tibia as well as in both olecranon processes. There are cystic areas in the proximal right femur indicative of defectively formed bones.

FIG. 3.—Sagging of the base of the skull over the cervical vertebrae and shortening of the neck.

FIG. 4.—Typical biconcave wedge-shaped and flattened osteoporotic vertebrae.

FIG. 5.—The typical triradiate pelvis, and cystic changes in the region of the lesser trochanter on the right side.

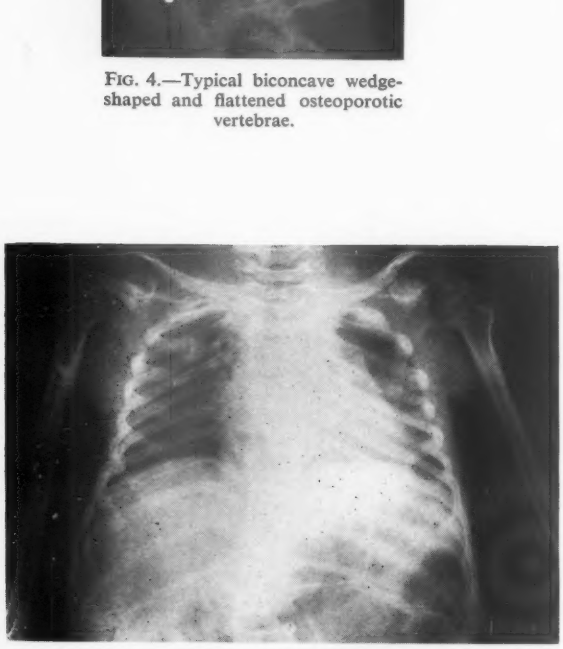

FIG. 6.—Note rib fractures. Spina bifida of T.1, T.2 and T.3. Looser zones present in both upper humeri.

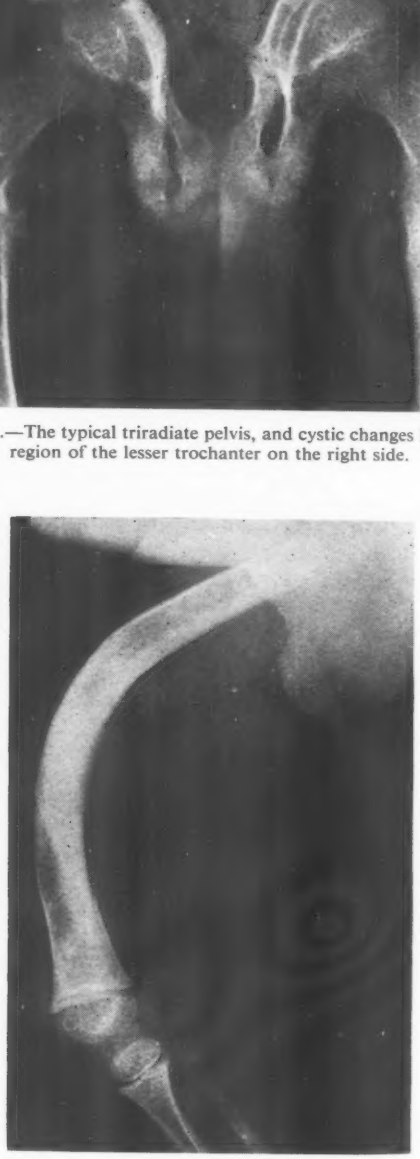

FIG. 7.—Typical bowing of the right femur.

Another striking feature is the relatively widened ends of the femora, humeri and tibiae (proximally in the latter).

Transverse lines of arrested growth are present in the long bones, especially marked in the distal portions of the humeri.

The clinical and radiological features of this case reveal it as an example of osteogenesis imperfecta tarda, because (1) there are no clinical or laboratory findings indicating any other osteoporotic condition. (2) There were no deformities at birth and the child played normally with other children until 4 years of age. (3) Fractures occurred comparatively late. The few are recent but most of the vertebrae are flattened. (4) The long bones are relatively well developed.

Case 2. E.S. is a European boy aged 3 years and is an example of osteogenesis imperfecta infantis of the post-natal thin bone type. He was a breech delivery, the head being delivered with forceps (weight 5 lb. 10 oz.) There is no mention of any fractures sustained during delivery. At the age of 2 months both upper arms fractured. No details are available. Two weeks later a fractured femur is recorded and *x*-ray examination at this stage revealed a uniting fracture of the other femur as well.

Apart from recurrent colds, sometimes accompanied by lung infections, E.S. was free from any illness.

His physical development was retarded; at 4 months he lifted his head, at 6 months he sat up. He has only been crawling for two months and with aid has been able to stand up for the last month. He speaks well, however, and appears to have normal intelligence.

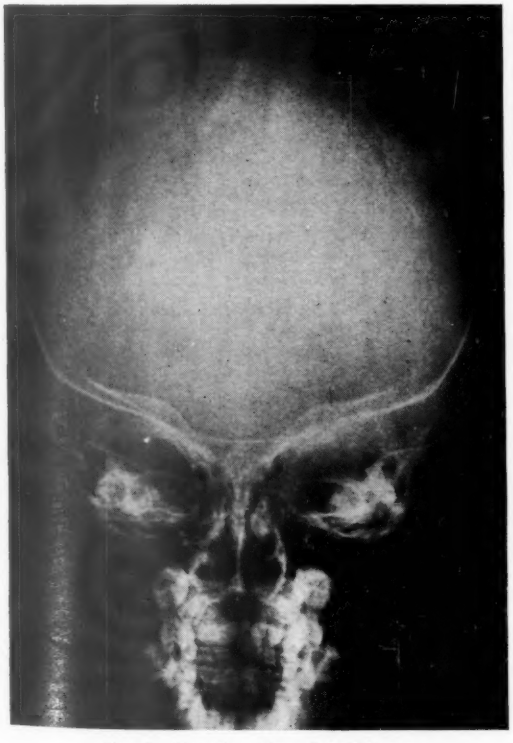

FIG. 8.—Pencil outline of skull bones.

FIG. 9.—Slightly curved slender bones of the upper extremities.

On examination he is found to be a frail little boy with a large round head and carious teeth. He has deep blue sclerotics, a depressed thoracic wall, long thin arms and legs with excessively mobile joints as a result of lax ligaments. Blood examination showed that the levels of calcium and phosphorus are normal.

RADIOLOGICAL FINDINGS. The skull bones are extremely thin and the skull is somewhat sagged upon the cervical spine (Fig. 8). The vertebrae are osteoporotic and somewhat biconcave but not compressed. The pelvis is normal. The limb bones are long and slender with narrow shafts and bossed epiphyses (Figs. 9 and 10). There is evidence of multiple united rib fractures, and fractures of the shafts of the long bones, which have united or are in the process of uniting. There is surprisingly little bowing and deformity of the long bones, vertebral column or thoracic cage in this case, but nevertheless it is radiologically a typical example of osteogenesis imperfecta infantis of the post-natal thin bone type.

Case 3. S.G. is a European boy aged 6 years and is another example of osteogenesis imperfecta infantis of the post-natal thin bone type.

He was admitted to the Pretoria Hospital with pneumonia on October 16, 1955. He had a tendency to recurrent colds and had a continual dry cough since drinking paraffin at the age of 19 months. He had sustained fractures on five occasions. At the age of 18 months, in 1951, he had fallen from a bed 2½ ft. high and sustained a fracture of the lower humerus. There

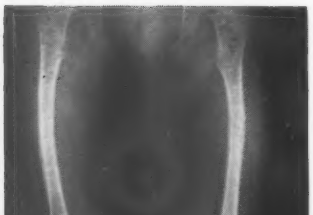

FIG. 10.—Slightly curved slender bones of the lower extremities.

FIG. 11.—Note blue sclerotics (dull white) and squint.

FIG. 12.—Note shortening of neck and spine. Arm in plaster, after recent supracondylar fracture.

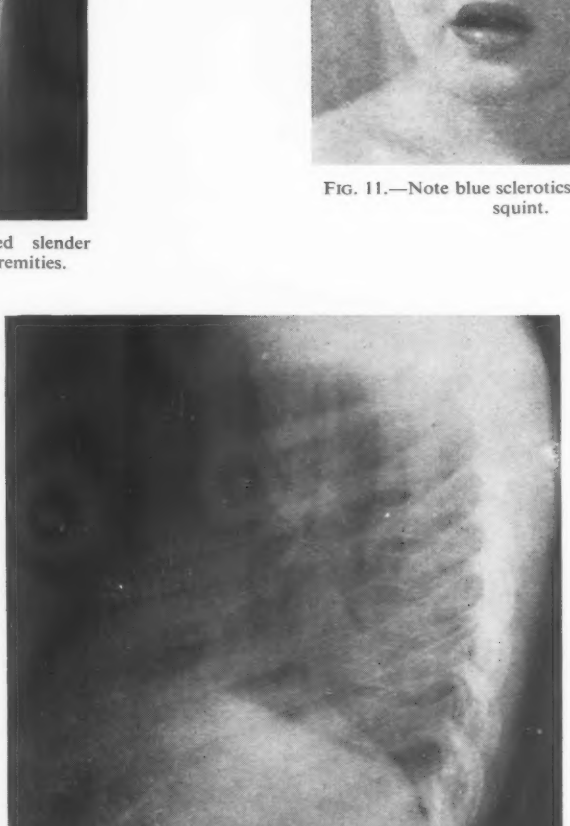

FIG. 13.—Osteoporosis of the vertebral bodies resulting in biconcave rather wedgeshaped thoracic vertebrae.

FIG. 14.—Plated supracondylar fracture. Note slender osteoporotic bones.

was malunion with external rotation and angulation of the distal fragment. In May, 1952, he refractured the right humerus at the same site as the result of a fall. Again there was malunion. In June, 1952, after falling, or slipping on a cement ffoor, he fractured the left tibia. Yet again he fractured his arm in October, 1952. In January, 1953, he was subjected to an operation for the correction of the shortening and external rotation.

On October 31, 1955, while in hospital for pneumonia he slipped on the stoep and fell, fracturing the right radius and ulna. The arm is still immobilized in plaster of paris.

According to his mother the trivial trauma causing his fractures would not have affected normal children.

After the lipoid pneumonitis in 1951 he developed a superior strabismus on the left side; an unsuccessful operation for correction of the squint was undertaken in November, 1954. His eye now deviates to the lateral and inferior side. He has no hearing defects.

Initially his physical growth was impeded by feeding troubles; at the age of 14 months he started walking and his intelligence is within normal limits.

FAMILY HISTORY. The father had no tendency to fractures, no deafness but has cardiomegaly.

The mother is aged 33 years and has a marked tendency to sustain fractures as a result of minor traumata. The first fracture occurred at the age of 7 years and the last in December, 1952. Since the age of 15 years she has been deaf in the right ear and this has steadily got worse.

Two other children, a daughter aged 3 and a son 5 months old, have, despite major injuries, never sustained fractures.

The father's family exhibit no tendency to sustain fractures or become deaf. The mother's father was deaf in the left ear, but never sustained fractures; her mother easily fractured her bones. Of the mother's five brothers and four sisters, all, except one brother and one sister, had sustained more than one fracture.

ANTE-NATAL HISTORY. S.G. was the first born and the mother had toxaemia from the sixth month and developed eclampsia at term. Labour was induced by rupture of the membranes and repeated injections. The delivery was normal and the baby cried lustily at birth. She remained well during the next two pregnancies.

EXAMINATION. On examination the patient was seen to be a young European boy, of fair nutritional state, but undersized for his age, with no anaemia, jaundice or cyanosis. He has blue sclerotics; pupil reflexes and fundi are normal. His left eye deviates externally and inferiorly and there is limitation of movement internally and superiorly. Lobar pneumonia (left base) had responded fully and rapidly to antibiotics.

The sedimentation rate was 4 mm. in the first hour (Westergren). The urine was negative for albumin; but microscopically pus cells, 1 r.b.c. per H.P.F., were seen.

A Mantoux test was negative (P.P.D. intermediate and second strength).

A blood count gave Hb 139/100 ml., W.B.C. 34,000 (staff cells 14%, polymorphs 65%, lymphocytes 15%, monocytes 6%). Blood platelets were normal.

The blood calcium level was 11·8 mg. %, phosphorus 1·7 mg. %, alkaline phosphatase 17·5 K.A. units. On repetition after this report was known blood calcium 10·7 mg. phosphorus 3·6 mg. %, alkaline phosphatase 16 K.A. units. In a 24-hour volume of urine 615 ml. calcium was excreted and 144·4 mg. per 24 hours.

RADIOLOGICAL FINDINGS. The skull bones are thin, and the skull sits on the cervical spine in 'tam-o'-shanter' style giving the appearance of a short neck (Fig. 12). The upper thoracic vertebrae show the typical osteoporotic appearance with biconcave compression of the vertebral bodies resulting in wedge-shaped vertebrae (Fig. 13). The pelvis is slightly deformed and compressed. The long bones are slender, and the cortex thin, but on the whole the skeletal ossification is much more substantial than in the other two cases. Multiple fractures are present, either united or in a stage of uniting. The right humerus is plated where there had been a recent recurrent fracture (Fig. 14).

Summary

Osteogenesis imperfecta is reviewed and a classification according to the radiological findings in the various age groups is given, together with a description and radiographs of three typical cases of osteogenesis imperfecta.

We wish to extend our thanks to Miss Campbell for the radiographs and to Mr. Theo Marais for the photographic reproductions of the radiographs and the other photographs of the patients, and to Dr. L. Pannall for particulars of E.S.

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A CASE OF GONADAL DYSGENESIS OR THE ULLRICH-TURNER SYNDROME WITH ANDROGENIC MANIFESTATIONS

BY

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This syndrome is thought to have been originally described by Ullrich (1930) and Turner (1938), but Meyer (1925) and Baer (1927) have given earlier descriptions of cases of 'ovarian agenesis' presenting with androgenic manifestations.

Grumbach, van Wyk and Wilkins (1955), in a thorough review of the subject, have proved the value of sex typing of nuclei in 22 cases, and by basing the same arguments as Russell, Levin and France (1955) on Jost's experimental work have suggested a partial explanation for the aetiology of this syndrome.

This report is of a child dying at 7 months, who had the cardinal features of the Ullrich-Turner syndrome associated with androgenic manifestations.

Case Report

Marion G. was the third child of healthy unrelated parents and was delivered normally at term after an uneventful pregnancy and labour. The mother had not received antenatal hormone therapy nor had she been exposed to *x* rays. The family history contributed nothing. The infant weighed 7 lb. 2 oz. at birth and despite obvious abnormality of the external genitals was considered to be female. The child was artificially fed but made poor general progress and was admitted to hospital on July 23, 1955, for investigations at the age of 7 months.

The infant was wasted (weight 11 lb. 4 oz.) and pale, being just under the average length for her age (25·5 in. against 26·6 in.). There was considerable coryza and some degree of inspiratory laryngeal stridor. The skull was brachycephalic (maximum circumference 16½ in.), the anterior fontanelle was widely open and the ears were prominent.

The following features of the Ullrich-Turner syndrome were present, some of which are illustrated in Figs. 1-3: Skin webbing of the posterior neck (Fig. 1), the skin being lax and thick; epicanthus, small mandible and high arched palate; broad chest ('shield chest') with hypoplastic nipples (Fig. 2); coarctation of aorta (loud praecordial systolic murmur, raised systolic blood pressure in arms (right 120 mm. Hg, left 125 mm. Hg) and absent femoral pulses); cubitus valgus and tapering fingers, the proximal and middle phalanges being swollen; pitting oedema of the dorsa of the feet.

A phallus (? enlarged clitoris) was present, 3 cm. long and covered with lax rugose skin (Fig. 3), apart from which the external genitalia were normal.

Sixteen days after admission the child developed fulminating bronchopneumonia and severe diarrhoea. There was no response to treatment and death occurred within 48 hours.

Laboratory investigations gave the following results: (1) 17-Ketosteroids in 24-hour specimen of urine, 2·2 mg. (normally less than 1 mg. at this age); (2) bone age 1 year approximately, i.e., slightly in advance of chronological age; (3) sex typing by the leucocyte method (Dr. W. M. Davidson), male, and by skin biopsy (Dr. J. B. Gibson) male.

Necropsy

A necropsy was performed on August 12, 1955, and the relevant findings are as follows:

There was marked left ventricular hypertrophy and the thicknesses of the right and left ventricular walls were 3 mm. and 11 mm. respectively. A 4-mm. segment of the aorta just distal to the opening of the ductus arteriosus (which was closed) was stenosed, the diameter of the lumen being reduced to 2 mm.

Small scattered areas of collapse were seen in the lungs.

The immature vagina, cervix, uterus and tubes were normally developed. At the ovarian sites were two flat, oval, yellowish structures (4 × 2 mm.).

Histology

In many areas of the lungs the alveoli were filled with a chronic inflammatory exudate.

The cortices of the adrenals were clearly defined and the bands of collapsed reticulin at the site of the X zone were evident (Fig. 4). The cortical lipoid content was not raised and there were no hyperplastic nodules. Broster-Vines, Ponceau-fuchsin stains gave negative results.

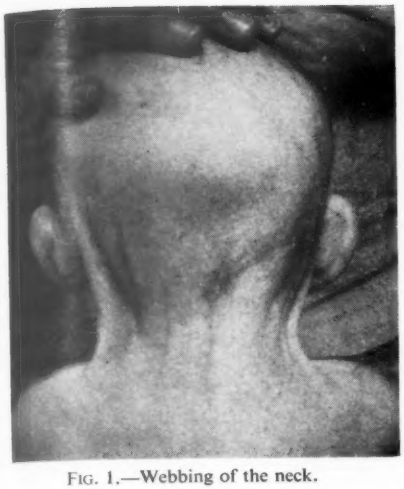

FIG. 1.—Webbing of the neck.

FIG. 2.—The epicanthus, prominent ears, 'shield chest' and hypoplastic nipples.

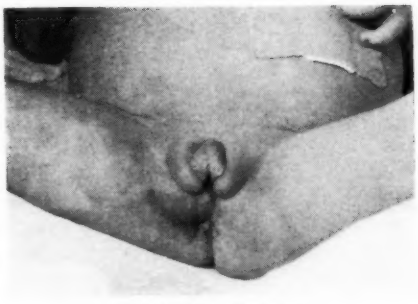

FIG. 3.—The phallus.

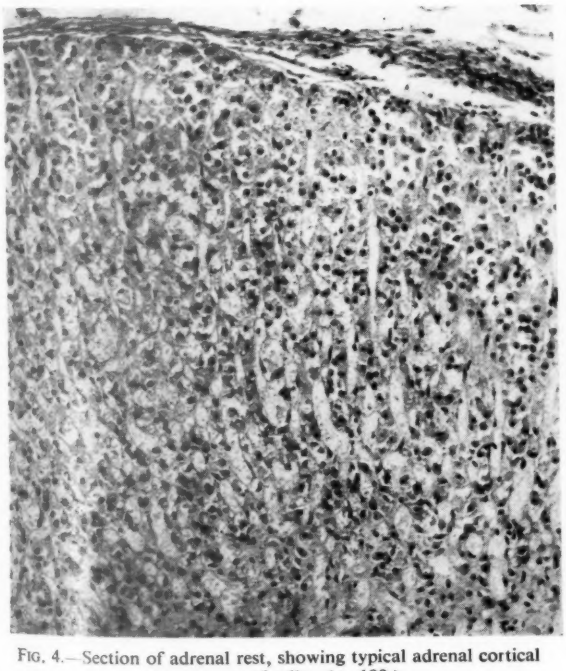

FIG. 4.—Section of adrenal rest, showing typical adrenal cortical arrangement of cells. (× 100.)

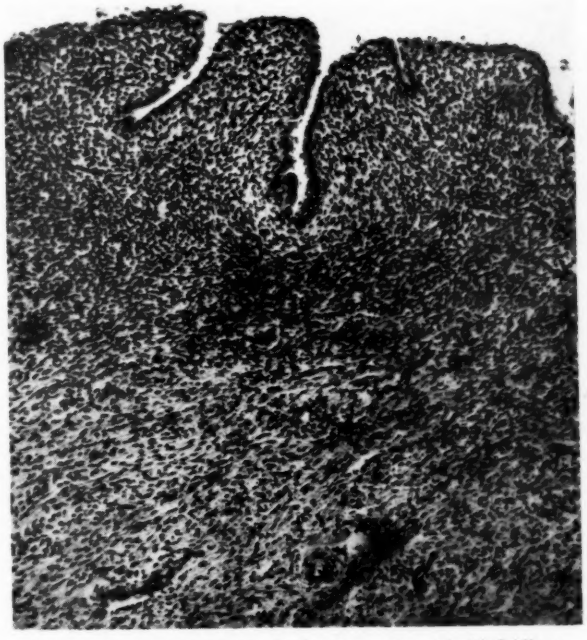

FIG. 5.—Section of uterine wall, showing endometrical infoldings. (× 100.)

The pancreas, thyroid, pituitary and thymus glands presented normal histological features. There was no evidence of Crooke's 'hyaline change' of the basophilic cells of the pars anterior of the pituitary (eosin-pyrrol blue stain).

The pre-tibial skin showed no evidence of myxoedematous change.

The centres and lines of ossification of the femoral, rib and vertebral bones had a regular pattern.

The phallus consisted of vascular fibrous tissue covered by normal skin. The labia majora consisted of fibrous tissue with normal overlying skin and no testicular elements were seen.

The appearances of the cervix, uterus and Fallopian tube were normal for this age and in the uterus small endometrial infoldings (Fig. 5) and an inactive stroma were easily distinguished. The structure at the ovarian sites consisted of well-differentiated adrenal cortical tissue (see Fig. 4), but the lipoid content of the cells was not raised and Broster-Vines, Ponceau-fuchsin stains were negative.

A section through one of the broad ligaments revealed a structure consisting of dense connective tissue resembling primary mesenchyme (or ovarian stroma). Scattered through this stroma were nests of large cells with ill-defined cell boundaries and with large round or oval vesicular nuclei containing two or three prominent nucleoli. Fine clumps of chromatin were scattered evenly throughout the nuclei. Nearer the surface were cords of large round cells with hyperchromatic nuclei and these cords lay parallel to the surface. No Leydig cells or vestiges of the mesonephros were present in this structure.

Discussion

This infant presented many of the features of this curious syndrome which suffers from a confusion of eponymous titles. The following alternative names have been suggested: Ovarian agenesis (Turner, 1938); status Bonnevie-Ullrich (symmetrical form) (Rossi, 1945; Oberman, 1955); pterygium (Skjelbred, 1953), or webbing syndrome of Ullrich-Turner (Russell *et al.*, 1955); gonadal dysgenesis (Grumbach *et al.*, 1955); Allbright's syndrome (Potter, 1952).

Rossi and Caflisch (1951), in a review of 68 cases, have listed 30 possible congenital abnormalities which may occur in this syndrome and in the present case 10 of these were found.

Sexing of the skin and polymorphonuclear leucocytes according to the method devised by Moore, Graham and Barr (1953) is now a recognized investigation in these cases (Polani, Hunter and Lennox, 1954).

The relatively frequent occurrence of coarctation of the aorta in this syndrome has been noted by some workers who have pointed out that this anomaly occurs with much greater frequency in males (8 : 1, Lewis, 1933; 5 : 1, Gould, 1953). The finding, by this method, that a high proportion of these patients are 'chromatin-negative', i.e., males, is therefore of great interest and in fact 20 of 22 cases investigated by Grumbach *et al.* were chromatin-negative and two patients in the chromatin-negative group had coarctation of the aorta. The present case is a further example of this association.

In their recent review of this syndrome Grumbach *et al.* have drawn attention to the experimental work of Jost (1947) on rabbits. Jost, performing intra-uterine operations, removed the foetal gonads at different phases in sex differentiation, beginning at a stage when the testis could be identified histologically, but the genital tract was still undifferentiated. In the female castrated foetus he showed that the Müllerian derivatives (female genital system) differentiated in a normal fashion apart from a slight reduction in size. In the male castrated foetus, on the other hand, the Wolffian derivatives (male genital system) failed to develop and instead a complete and normal female genital system developed in its place. Unilateral castration of the male foetuses caused the Müllerian derivatives on the castrated side to develop in place of the Wolffian system. It would seem, therefore, that the all-important factor in sex differentiation of the genital tract is the presence of some locally acting tissue 'organizer' secreted by the male gonad. Jost has further shown that castration of the male rabbit foetuses at successively later stages allows increasing degrees of differentiation of the Wolffian derivatives but arrests their further development. Beyond a certain stage, however, castration of the male foetus will fail to prevent normal development of the Wolffian system. Grumbach *et al.* regard these patients with gonadal dysgenesis as the human counterparts of the castrated rabbit foetuses and suggest that some deleterious agent of unknown nature affects the embryos. In the case of the human male this would have to occur before the 28 mm. embryo stage (eighth week) in order to prevent differentiation of the male genital system. The associated malformations in this syndrome could also be determined at this stage (Grumbach *et al.*).

It would be attractive to align the present case with its androgenic manifestations with one reported by Grumbach *et al.* in which there was phallic enlargement and to suggest, as do these authors, that these cases correspond to the male rabbit foetuses of Jost which have been castrated at an intermediate stage.

Meyer (1925), Baer (1927), Pich (1937), del Castillo, de la Balze and Argonz (1947), Russell and Swyer (1952), Gordan, Overstreet, Traut and

Winch (1955), Grumbach *et al.* (1955), Greenblatt, Carmona and Higdon (1956) have all recorded cases of this syndrome with androgenic manifestations. In five of these cases there has been a histological examination of a 'genital ridge', found in the broad ligament at laparotomy, and this has shown in each case the presence of nests of Leydig (hilar) cells scattered through a connective tissue stroma closely resembling that of the ovary. With the exception of Greenblatt *et al.*, the authors correlated the presence of these cells with the androgenic manifestations, but admitting at the same time that they are found in cases without any evidence of masculinization. Greenblatt *et al.* were unable to allow the possibility of this correlation in their case because the androgenic manifestations occurred in association with low urinary 17-ketosteroids.

The histological appearance of the structure in the broad ligament of this case, and the absence of any specific features which would enable one to identify it as a primitive testis or ovary, suggest that it represents undifferentiated gonadal tissue (Gillman, 1948). However, no Leydig cells could be found in this 'genital ridge' and it seems preferable, therefore, to relate the phallic enlargement, bone age maturity (usually retarded in this syndrome) and the slightly elevated 24-hour urinary 17-ketosteroids to adrenal hyperplasia.

It is of interest here to note that ' . . . in the male animal castration is followed by adrenal cortical hypertrophy' (Soffer, 1951). There was, however, no morphological evidence of adrenal hyperplasia in the present case, apart from the presence of heterotopic adrenal tissue, but correlation of the structural changes in the adrenal cortex with its biological activity is difficult and histochemical stains for 17-ketosteroids are not specific (Pearse, 1953).

In Baer's case, a 23-year-old 'female' with a male habitus and sexual infantilism came to laparotomy and was found to have bilateral adrenal rests at the usual ovarian sites, no ovaries being present. Baer also attributed the androgenic manifestations to the ectopic adrenal tissue. In the human embryo at the 12 mm. stage the genital ridge and suprarenal ridge lie in continuity, therefore it is easily understood that heterotopic adrenal cortical tissue can appear in relation to the usual gonadal sites, as seems to have happened in the case reported here and in Baer's case (Hamilton, Boyd and Mossman, 1952).

Summary

A case of 'gonadal dysgenesis' in a male ('chromatin-negative'), aged 7 months, is described.

Recent theories concerning the aetiology of this syndrome are outlined and the possible cause of the androgenic manifestations in this case is discussed.

We wish to thank Professor F. M. B. Allen, under whose care the child was admitted, and Dr. G. Rutledge for his help with the clinical care of the child; Professor J. H. Biggart for his helpful advice; Dr. W. M. Davidson, Dr. E. F. McKeown and Dr. J. B. Gibson for the nuclear sex typing; Drs. A. Russell, N. E. France, W. R. N. Morton, J. E. Morison and H. B. McDowell for advice on various aspects; Mr. D. Mehaffy and Mr. R. Wood for photographs; Miss P. Stewart for secretarial assistance; and the resident medical and nursing staff of the Royal Belfast Hospital for Sick Children for their assistance while the child was in hospital.

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CYSTIC DISEASE OF THE LUNG IN THE NEWBORN TREATED BY PNEUMONECTOMY

BY

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From the Royal Aberdeen Hospital for Sick Children

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Congenital cystic disease of the lung is an uncommon condition which may remain asymptomatic for long periods or may, at any time, become potentially lethal either as a result of infection or of increasing tension in the cysts. Infection is a constant danger whenever a cavity communicates with the bronchial tree and is responsible for the development of symptoms in a considerable number of cases. Ravitch and Hardy (1949) found evidence of infection in every one of 12 lung cysts excised in childhood. That infection may arise at a very early age is shown by the third case of Swan and Aragon (1954) in which a large air-containing cyst, shown radiologically at the age of 6 days, had been transformed into a tense abscess two weeks later. In early infancy, however, acute symptoms are more often produced by rising tension in the cysts and it seems that, if this complication is to develop during childhood, it nearly always does so in the first year, and, indeed, in the majority of cases, during the first few weeks of life. The early diagnosis of tension cysts has assumed increasing importance since it has been realized that surgical treatment can retrieve or prevent the desperate situation which may arise when a valvular obstruction in the bronchus causes the cysts to balloon thus increasing compression of the normal lung tissue.

The first successful resection for this condition in a young infant was reported by Fischer, Tropea and Bailey (1943). Swan and Aragon (1954) reported three successful resections for congenital cystic disease of the lung and quote references to 15 other resections in infancy after the original case of Fischer *et al.* In 15 of these 19 cases symptoms were due to increasing tension in the cysts. In addition we have found reports in the British and American literature of a further nine cases of tension cysts in infancy treated by resection (Walker, Taggart and Staton, 1948; Strode, Case 2, 1949; Dugan and Samson, Cases 1 and 4, 1950; Hill, 1951; Whitesell and White, 1952; Belcher and Siddons, three cases, 1954). Of this total of 24 cases, 21 were subjected to lobectomy and three to pneumonectomy with only one post-operative death (Strode, 1949) and a satisfactory functional result in all other cases.

The fact that only four of these 24 resections were performed in Great Britain (Belcher and Siddons, 1954; Crowe, 1954) has prompted us to report the following case to draw attention to the possibilities of radical surgical treatment at an extremely early age.

Case Report

Baby S.C. was the first child of healthy parents, born on November 10, 1954, by low forceps delivery after an uneventful pregnancy and a labour lasting 12 hours. Her birth weight was 7 lb. 4 oz. and her condition at birth was satisfactory. During the third day her breathing became laboured and she was transferred to the Royal Aberdeen Hospital for Sick Children. On admission her general condition was satisfactory, she did not appear distressed despite a respiratory rate of 80 per minute and she showed no cyanosis. On examination it was apparent that the heart lay in the right chest; the left chest showed little respiratory movement and was hyper-resonant with weak breath sounds, while normal breath sounds were heard on the right side. Physical examination was otherwise negative. A radiograph of the chest (Fig. 1) showed marked displacement of the mediastinum to the right and only a small area of aerated lung was visible on that side; in the left hemithorax clearly defined cystic spaces occupied almost the whole lung field. While the appearances were suggestive of multiple tension cysts in the left lung it was felt that the possibility of diaphragmatic hernia could not be absolutely excluded and, on the following day, a barium enema, and subsequently a small 'dionosil' meal were given; the gastro-intestinal tract was shown to be normally situated.

After admission the respiratory rate fell to 50 to 60 per minute and as the infant was not distressed and was able to take her feeds no immediate treatment was considered necessary. Her condition remained unchanged until the afternoon of November 19 when she became very dyspnoeic and cyanosed. Thirty-five millilitres of air

were aspirated through a needle in the left anterior axilla with some immediate improvement. It was impossible to withdraw more air from this site and the needle was removed. Two hours later she again became very dyspnoeic and appeared *in extremis*; the left chest was again aspirated, and by altering the position of the needle from time to time it was possible to remove 190 ml. of air; from no one position was it possible to aspirate more than 30 to 40 ml. which suggested that the cysts did not inter-communicate very freely. This aspiration produced considerable improvement but it was clear that any advantage gained in this way was likely to be temporary and that catheter drainage would not produce satisfactory decompression. It was, therefore, decided that immediate resection of the cystic lung was the only possible course. One further aspiration was necessary while she was being prepared for operation. A radiograph of the chest immediately before operation showed little change; if anything, the mediastinum was displaced even further to the right than in the initial radiograph.

Operation was undertaken (F.J.S.G.) on the evening of November 19, when the child was 9 days old. Premedication was with atropine, grain 1/200, and after an open ether induction, a gum elastic catheter was passed into the trachea and the lungs inflated with pure oxygen plus occasional traces of ether. The anaesthetic presented much greater difficulty than the operation; it was impossible to maintain a good colour,and inflation remained difficult after the lung was removed, presumably because of partial atelectasis of the right lung.

The left chest was opened in the fifth intercostal space with the infant in the lateral position. The lung was bulky and did not deflate normally. The upper lobe was small and atelectatic, and only a rudimentary fissure was present. As speed was essential, no attempt was made to preserve the upper lobe, and dissection pneumonectomy was carried out. The bronchus stump was closed with interrupted nylon sutures and covered with pleura. The chest was closed in layers without drainage, the pleural pressure being adjusted by means of a needle to a mean minus 5 cm. of water after the infant had been turned on her back.

On return from the theatre her general condition was poor and she required continuous oxygen. Twelve hours later she was crying quite lustily and her respirations were much easier though her colour still deteriorated when oxygen was withheld. A radiograph showed comparatively little expansion of the right lung. The pressure in the left pleural cavity was found to be + 2 to + 18 cm. of water; 260 ml. of air was aspirated, leaving a final pressure of − 11 to 0 cm. water. Further aspirations of 80 ml. that evening and 20 ml. next morning (November 21) maintained a satisfactory negative pressure and by November 22 radiography showed the right lung well expanded and apparently normal and the mediastinum well over into the left chest, which now contained an effusion. It was now possible to stop the administration of oxygen and her respirations remained easy and her colour good. Twenty-five millilitres of blood-stained fluid were aspirated from the left chest on November 27, but thereafter no further aspiration was necessary. Radiographs taken at intervals until her discharge from hospital on December 18 showed further shift of the mediastinum to the left and considerable elevation of the left diaphragm. She remained rather hypotonic and easily tired, and catheter feeding was necessary until a few days before her discharge; her general condition then improved and she began to take her feeds by bottle.

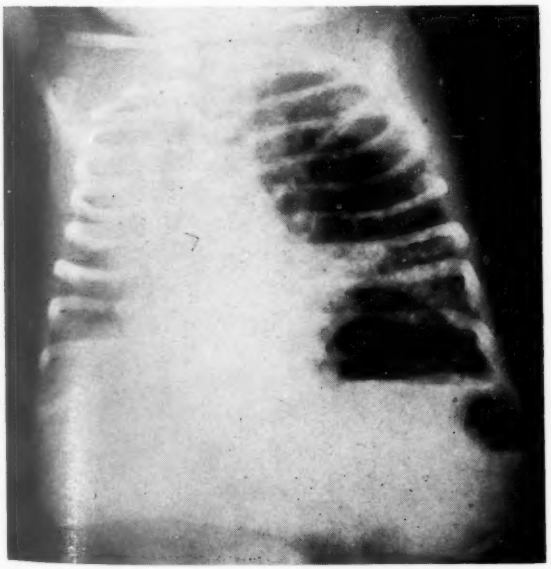

FIG. 1.—Age 3 days. Gross mediastinal displacement by air-distended cysts in the left lung.

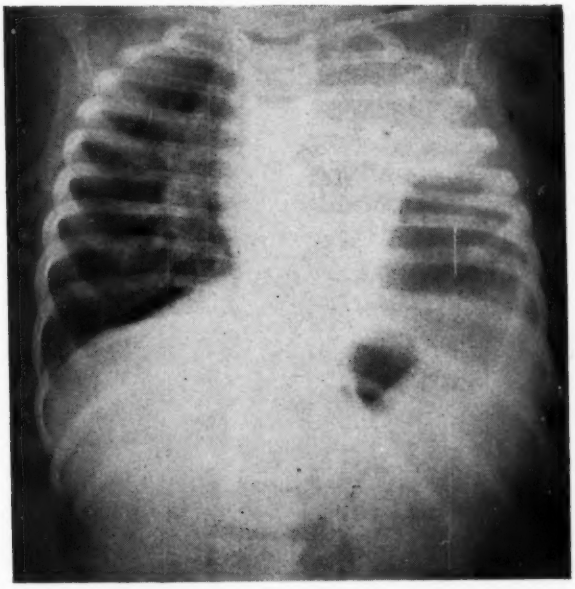

FIG. 2.—One year after operation. The left diaphragm has risen considerably and the mediastinum has moved further to the left.

Her progress at home, although slow at first, was steady, and by the age of 4 months she weighed 12¼ lb., looked well and held her head up steadily. At the age of 1 year she weighed 20¼ lb. and looked a normal child with a remarkably symmetrical chest and no sign of scoliosis. She could stand with minimal support, was not dyspnoeic and had thrown off several respiratory infections without difficulty. A radiograph of the chest (Fig. 2) showed considerable displacement of the mediastinum to the left and marked elevation of the left cupola of the diaphragm; the right lung appeared normal.

Pathology. The resected lung was fixed before examination by introducing formol-acetate into the bronchial tree under slight positive pressure and tying off the main bronchus. Transection showed diffuse cystic change in the lower lobe except for a small area in the apical segment which was atelectatic (Fig. 3). The upper lobe was poorly developed and not well demarcated from the rest of the specimen; it had a similar appearance to the apical segment of the lower lobe. The cysts in the lower lobe varied in diameter from the lower limit of visibility up to 3 cm.; the lining of the larger ones was often trabeculated as though they had been formed by the confluence of several smaller cysts.

Microscopical examination showed that the cystic spaces were bronchiectatic in nature. They were lined mainly by ciliated columnar epithelium which was pseudostratified in some places; occasionally the epithelium was cuboidal and it was more or less deficient where the cysts opened into alveolar ducts. Normal-looking alveoli were found between the cystic spaces (Fig. 4). The atelectasis in the airless upper zones was confirmed; the lung tissue here showed foci of maldevelopment in which the parenchyma appeared to be of foetal type and there were also areas of alveolar haemorrhage.

In view of the special interest of the case a more detailed histological examination of the lung was made to try to decide the pathogenesis of the cysts and also the cause of their valvular inflation. Large serial sections, 25μ thick, were cut from the whole of the upper half of the specimen illustrated in Fig. 3. Two hundred and fifty of these sections were stained alternately with haematoxylin and eosin and Verhoeff's elastic stain counterstained by van Gieson's method. Extra sections from here and elsewhere in the lung were stained for special features by Foote's silver method, by the per-iodic-acid-Schiff method, and by Gram's method. The following observations were made from study of these sections. Most of the cysts looked like dilated bronchioles in that they showed no cartilage in their walls; some appeared to be dilated respiratory bronchioles since they were lined partly by cubical epithelium and opened directly into alveolar ducts. The cyst walls were often lax and showed many convolutions and papillary foldings. Deep to the epithelium the wall consisted of fibrous connective tissue with abundant elastic; smooth muscle was recognized but was inconspicuous. The lumina of the cysts were part of the air conducting system of the lung, communicating proximally with the main bronchi and peripherally with alveolar ducts, alveolar sacs and alveoli. The alveolar ducts were sometimes distended, but the air sacs themselves, although showing more variation in size than usual, were in no respect cystic; for the most part they looked normal. A few of the alveoli and cystic spaces contained fresh blood, possibly from the operation or the pre-operative chest punctures. A further notable feature was the presence of broad trabeculae of loose connective tissue, dividing the lung into large lobules. There was no positive evidence of prenatal aspiration of amniotic fluid: typical squames could not be identified either in haematoxylin-and-eosin preparations or in the Gram-stained sections. The main vessels and bronchi looked normal apart from certain striking changes near the origins of the segmental bronchial branches: here there was definite evidence of bronchial stenosis. A model made from tracings of photographic magnifications of this area confirmed the presence of a severe stenosis; it was a flattening rather than a uniform constriction and in some ways suggestive of a twist rather than of a compression (Fig. 5). Such a degree of stenosis could readily act as a check valve (Jackson and Jackson, 1952) and cause progressive inflation of the lung beyond.

Discussion

Pathogenesis. The classification and development of cystic changes in the lung have been discussed in detail by several authors (Koontz, 1925; Sellors, 1938; Kjaergaard, 1935; Willis and Almeyda, 1943), but perhaps the simplest concept of the mechanisms producing pulmonary cysts in the newborn is that of Anspach and Wolman (1933) who suggested that the cysts may be (*a*) preformed but collapsed, expanding with the first respiration; (*b*) small congenital bronchiectatic dilatations which expand with respiration if there is a concomitant check-valve deformity in the air passages; (*c*) fluid cysts which become air-filled after birth once the fluid is evacuated. It is to category (*b*) that our case seems to belong, since it shows undoubted bronchiolectasis together with check-valve deformities in the bronchi. An element of bronchiolectasis appears to have been present for some time before birth because the walls of the cystic cavities were in many places lax and thrown into folds indicating the growth of extra tissue here. Such an increase in bronchiolar dimensions could hardly have arisen in the few days of post-natal life simply from the effect of the valvular anomaly exposing normal-sized bronchioles to increasing air tension. There is also indirect evidence for this view from the observations of Robertson and James (1951) and Weisel (1955) that valvular bronchial stenosis alone is associated with diffuse lobar emphysema, not dilatation of bronchi or bronchioles. Thus it is clear that, while the valvular bronchial stenosis in our case must have

FIG. 3.—Lung transected coronally to show multiple cysts in the lower lobe; the apical segment of the lower lobe and the entire upper lobe are maldeveloped and atelectatic. (Two-thirds size.)

FIG. 4.—Section of the lower lobe showing cysts lined by respiratory epithelium and opening into alveolar ducts; the alveoli between the cysts contain some fresh blood but look otherwise normal. (Haematoxylin and eosin. ×60.)

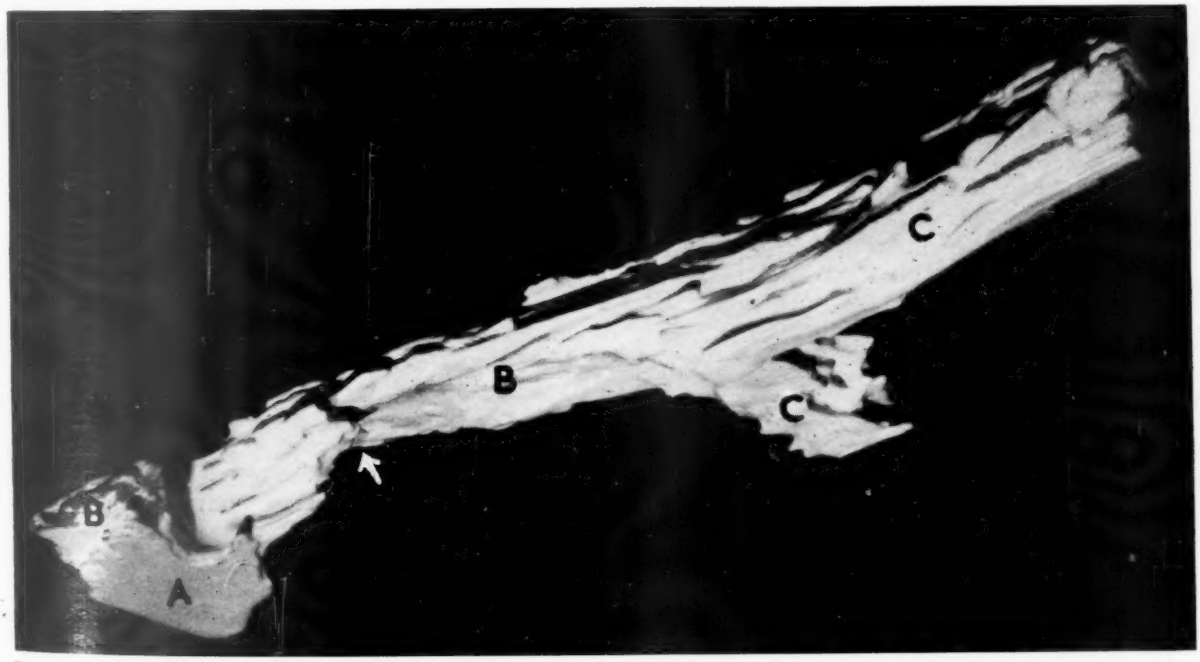

FIG. 5.—Model constructed from tracings of photographic enlargements of the serial sections from the posterior basal segmental bronchus region. The basal bronchus (A) is seen branching into its anterior and posterior branches (B). The latter shows the stenosis marked by the arrow, and gives rise to two subsidiary branches (C). (× 20.)

been of prime importance in the production of the increasing intrathoracic tension after birth, it probably played no part in the production of the weakening and overgrowth of the bronchiolar walls. In theory, it might be supposed that such a stenosis could lead to cystic lung changes *in utero* from the progressive aspiration of amniotic fluid, but, in fact, this is a most unlikely explanation since intrauterine breathing in human infants is no more than a hypothetical occurrence; moreover, in our case there was no evidence of aspiration histologically and no sign of residual fluid in the cysts when the child was radiographed at 3 days old.

It seems likely that the bronchial anomaly, the bronchiolectasis and the partial dysplasia of the upper zones of the lung were all parts of a general, but unilateral, pulmonary developmental disturbance. The timing of this maldevelopment can now only be a matter for speculation but if the bronchial anomaly is in fact a torsion defect, as is hinted by its appearance, then this is likely to have occurred at a very early stage of foetal life while bronchial branching was still minimal. Perhaps a concomitant local anomaly of blood supply resulted in the defective development elsewhere in the lung; but evidence for such a speculation is lacking. It seems highly probable, however, that the changes in the cystic lung had a local cause because the opposite lung was not similarly affected.

Diagnosis. Although this condition is uncommon its diagnosis should rarely present difficulty. The essential clinical features are dyspnoea in an infant showing impaired respiratory movement, distension, hyper-resonance and poor air entry over one side of the chest with gross displacement of the mediastinum into the opposite side of the chest. Radiographs may show a single 'balloon' cyst or, as in the present case, multiple cystic spaces occupying most of the affected side of the chest.

Pneumothorax, congenital lobar emphysema and diaphragmatic hernia are the only other abnormalities which can produce rather similar clinical or radiographic pictures. Pneumothorax and congenital lobar emphysema produce a clinical picture indistinguishable from that of tension cysts but the radiographic appearances are usually diagnostic. In diaphragmatic hernia the percussion note on the affected side will usually be impaired rather than hyper-resonant but the physical signs may be otherwise identical. Multiple cysts, as in the present case, may produce a radiographic picture resembling that of the bowel gas shadows in diaphragmatic hernia but the distinction can easily be made with the aid of an opaque meal or enema. Failure to carry out this investigation resulted in laparotomy in two of the 24 cases quoted in the introductory paragraphs before the correct diagnosis was reached.

Management. Caffey (1953) maintains that lung cysts in infancy usually regress spontaneously and should always be treated expectantly except in 'the rare case of acute respiratory obstruction due to sudden and marked expansion of the cysts'. It is clear, however, that in nearly all the cases described in his paper the cysts followed pneumonia. Cysts of this type are by no means uncommon and it is generally agreed that they are usually benign and tend to disappear spontaneously. Caffey appears to believe that there is no fundamental difference between the two types of cyst, but we have found no convincing evidence that cysts found in the first week or two of life in the absence of infection behave in the same way as post-pneumonic cysts. It is certain that some of them will become infected and that some will become ballooned. Whether any of them disappear or remain benign and symptomless throughout life we do not know, but it seems highly probable that, if they escape the danger of over-inflation, the ultimate risk of infection must be very high. Perrott (1956) has described 17 cases of cystic disease of the lung, 15 of them aged 20 years or more; virtually all of them had signs or symptoms of infection and the majority were severely disabled. Until we know more of the natural history of these cysts it is impossible to say whether resection is justified in every case even in the absence of acute symptoms. It seems probable, however, that in the present case which showed gross mediastinal displacement, operation should have been performed earlier despite the fact that signs of respiratory distress became less severe after the baby's admission to hospital. The operation might well have been less hazardous had it been performed immediately the diagnosis was confirmed; the temptation to temporize while the symptoms seemed less acute should have been resisted and surgical advice sought at once.

Evidence of progressive compression of functioning lung by distension of congenital cysts is an absolute indication for immediate resection of the affected lung or lobe. Thoracotomy and lung resection are tolerated amazingly well by very young infants, and present no serious technical difficulties. Delay is likely to increase the dangers of operation owing to the anaesthetic difficulties which result from compression of normal lung tissue. In the present case we did not know whether the right lung was structurally normal as it was almost completely collapsed when the first radiograph was taken, but it appeared

that left pneumonectomy offered the only hope of saving the child's life. Resection is the only measure which will at the same time relieve the immediate danger and offer prospect of permanent cure. Aspiration of the cysts is a useful expedient while preparations are made for operation, but, as Albert and Potts (1953) point out, it is never an elective procedure and is always followed by re-inflation of the cysts and often by pneumothorax. They also emphasize that 'when a definitive diagnosis of expanding lung cyst has been made and confirmed by roentgenographic examination, the infant is literally followed by a physician with a large syringe and needle in his hands while preparations are being made for surgery'. We had not read this paper before dealing with the present case, but were rapidly forced to the same conclusion and the precaution they suggest was in fact taken, almost to the letter.

Summary

An infant with congenital cystic disease of the lung developed acute respiratory distress at the age of 3 days as a result of progressive distension of the cysts. Symptoms became much more severe at the age of 9 days and pneumonectomy was performed with an excellent functional result. Although lobectomy has been performed for this condition at an even more tender age, it is believed that the present patient is the youngest to undergo pneumonectomy.

Examination of the resected lung showed the cysts to be dilated bronchioles which in some cases opened directly through alveolar ducts into alveoli. The evidence suggested that some bronchiolar dilatation was present before birth. The segmental bronchi serving the affected areas of the lung showed localized stenoses which presumably acted as check-valves with consequent ballooning of the cysts.

Attention is drawn to the importance of the early recognition of expanding lung cysts in infancy, a condition which, if untreated, is likely to prove rapidly fatal. A survey of the literature has shown that the results of early surgical resection are highly satisfactory.

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THE SCHÖNLEIN-HENOCH SYNDROME WITH PARTICULAR REFERENCE TO RENAL SEQUELAE

BY

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In recent years the Schönlein-Henoch syndrome has been discussed in many articles and particular interest has centred around the incidence and outcome of renal complications. As long ago as 1899 Henoch stated that nephritis was a frequent complication which might progress to anasarca and prove fatal. In a recent series, Wedgwood and Klaus (1955) found that, of 26 cases followed for periods between two and 15 years, 10 children had abnormal urine, only six of these having had proteinuria or haematuria during the acute stage of the disease. These authors, therefore, believe nephritis may occur as a late sequel in some cases even when urine examinations showed no abnormality during the acute stage. On this basis it has been postulated that the Schönlein-Henoch syndrome might be considered as a possible latent cause of nephritis in older children and adults. Oliver and Barnett (1955), on the other hand, say that, although renal involvement occurs in approximately half the children with anaphylactoid purpura, their follow-up results indicate that nephritis does not emerge as a late sequel.

In 1952 we published a series of 35 typical examples of the Schönlein-Henoch syndrome, seen between the years 1943 and 1950, together with four cases which were atypical but which appeared to be related disorders of the collagen system (Derham and Rogerson, 1952). It is now proposed to review the progress of as many of the original cases as it has been possible to trace and to report a further 59 cases which have been admitted to Alder Hey Children's Hospital, Liverpool, from 1951 to 1955. The earlier cases have been reviewed in an attempt to determine the incidence of renal complications. Addis counts and urea clearance tests have been carried out in 34 patients taken from the two series, irrespective of whether they had, or did not have, renal complications at the time of their original illness.

Follow-up of 1943-50 Series

Of the original 35 typical cases admitted between 1943 and 1950, nine had haematuria and another 10 had albumin and red cells in their urine while they were still in hospital, a total of 19 (54%) with renal involvement of varying degree. At the time of their discharge from hospital 15 of these children had clear urine whilst four still had albumin and red cells. Of these four children, three had no other clinical evidence of nephritis and they are now quite well. One child has had considerable albuminuria for eight years but is now recovering and recent renal function tests give normal results.

Some of the patients in this series have left the district, but 17 of the 35 have been traced. It has been found that nine of them have had no recurrence of any symptoms, five report occasional joint pains and swelling, one has had the rash on one occasion with joint swellings, pain and colic, and two have had frequent recurrences of the rash, together with abdominal pain and swelling of ankles.

Urea clearance and/or Addis counts have recently been carried out for 14 of the patients, including the two children with frequent recurrences. These tests gave normal results in 10 instances. Two patients, girls of 13 and 19 years, showed a mild impairment of kidney function, one girl of 18 years had moderately impaired function and one other girl of 15 years has a severe deficit. This last case was complicated by a recent nephrectomy for hydronephrosis.

Four Atypical Cases in the 1943-50 Series. The four cases reported, which were described as 'atypical', had some of the clinical manifestations of the Schönlein-Henoch syndrome associated with other aspects of collagen disease. One child (Brian J., Case 4) had already died from periarteritis nodosa when the cases were reported. Of the remaining three cases, two are well and one has died. These three cases were as follows:

TABLE 1
SCHÖNLEIN-HENOCH SYNDROME CASES ADMITTED TO ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL, 1943–1955

	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954	1955	Total
Males	1	2	2	1	4	2	4	2	3	6	10	8	6	51
Females	–	1	–	3	–	6	6	1	5	5	5	4	7	43
Total	1	3	2	4	4	8	10	3	8	11	15	12	13	94

Case 1 (Rodney McW.). This boy was 5½ years old when he was admitted to hospital in 1949 with haematuria, abdominal pain, vomiting, swelling of joints, a purpuric rash and a history of asthma. The rash became so necrotic that local areas of gangrene appeared. This child had a long, severe illness, lasting five months and, when discharged, still had persistent albuminuria but no hypertension. During the succeeding six years he has had five purpuric episodes and frequent asthmatic attacks. Despite the recurrences, his kidney function, as shown by urine examinations, blood urea, Addis count and urea clearance tests, is normal.

Case 2 (Jeanette D.). When first admitted to hospital in 1950, this girl had had recurring purpura on the arms and legs and joint swellings for the previous three years. She developed subcutaneous nodules while in hospital. Skin biopsies presented the histological appearance of disseminated lupus erythematosus and muscle biopsy showed panarteritis with thrombosis, recanalization and cellular infiltration of the walls of vessels. No abnormality was found in the urine. This patient is now 20 years of age and works as a cinema usherette. She is in good health, has had no recurrences, and recent kidney function tests show no abnormality.

Case 3 (Beryl R.). This girl, aged 9½ years, had eight episodes of abdominal colic and haematuria in 12 months. Her widespread rash resembled erythema marginatum, but the clinical picture suggested a relationship with the Schönlein-Henoch syndrome. She was in hospital for six months and, after discharge, continued to have albuminuria. Two years later she was readmitted with haematuria and developed hypertension, general oedema, ascites and pleural effusions. She died with a terminal pericarditis. At necropsy, the kidneys were large and pale. Histologically, the picture was that of a mixed Ellis type I and type II nephritis.

Present Series, 1951-55

During the five-year period, 1951-55, another 59 undoubted examples of the Schönlein-Henoch syndrome were seen in Alder Hey Children's Hospital. These, with the previous series of 35, make a total of 94 cases. There were 51 males and 43 females (Table 1), a ratio of 1·2:1, which is a slightly higher proportion of females than the ratio of 2:1 found by Oliver and Barnet (1955) and higher also than the 3:2 ratio in the 139 cases recorded by Lewis (1955).

In the present series the youngest child was aged 20 months and the oldest 14 years: both were girls. Nearly half the total number, however, fell into the age group 5-7 years (Table 2).

TABLE 2
SCHÖNLEIN-HENOCH SYNDROME CASES ADMITTED TO ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL, 1943-1955

Age Groups	Number of Cases
Under 5 years	10
5–7 ,,	27
8–10 ,,	13
11–14 ,,	9
Total :	59

Two deaths occurred. One, a girl aged 11 years, died 10 weeks after admission from cardiac failure and chronic nephritis. She had had five recurrences of the rash and repeated attacks of colic and haematuria during her illness. Unfortunately, permission for necropsy was refused. The other child was a boy, aged 6 years, who died of uraemia 11 weeks after admission. He had had a purpuric rash, abdominal colic and joint swellings on admission, but did not have any renal complications until two weeks later, when he developed albuminuria, haematuria, anuria and hypertension, and eventually died from uraemia. Post-mortem examination was carried out in this case; the kidneys were pale and histological examination showed advanced changes of chronic glomerulonephritis.

There was no very marked seasonal incidence in the occurrence of these 59 cases of the recent series. As might be anticipated, a majority of the children were admitted during the winter months (October-March, 34 cases; April-September, 25 cases). The length of stay varied considerably, depending mainly upon the presence or absence of renal involvement. Other factors, such as recurrence of rash, joint swelling and abdominal colic and social aspects, played less important parts in prolonging their stay in hospital. The average length of stay was nine weeks, but those with gross urinary changes remained for 21 weeks (average).

Clinical Findings in the 1951-55 Series. The following are the most outstanding:

TONSILLITIS. Only 15 of the 59 patients complained that they had had a recent sore throat, but a throat swab was always taken on admission and in 20 cases haemolytic streptococci were isolated. In one child with suspected intussusception, the throat swab remained sterile but a swab taken from a laparotomy wound grew haemolytic streptococci. Group typing was carried out in only three cases, the results being: type 5 (two cases) and type 19 (one case).

RASH. The typical purpuric rash, as described by Gairdner and other writers, was present in every case, but in 19 patients it was not the first manifestation: 10 children had joint swelling and nine had abdominal pain before the rash appeared. In one case the rash was so severe that necrosis occurred.

JOINT SWELLINGS. These occurred in 35 cases: in 20 of these more than one joint was affected, the commonest being the ankle and knee.

ABDOMINAL COLIC. Abdominal colic occurred in 30 cases. Four were submitted to laparotomy: in three the presenting symptom on admission had been abdominal pain of such severity that an acute surgical condition had been diagnosed. At operation petechial haemorrhages were seen on the intestinal walls, but in each case skin purpura appeared only after an interval of several days. The fourth case developed an intussusception one week after admission with rash and swelling of the ankles. The intussusception was reduced at operation.

In addition, two other children had signs of intestinal obstruction and abdominal radiographs showed fluid levels. Both these patients had severe colic, vomiting and haemorrhage from the bowel, but both recovered without surgical intervention.

BLEEDING. Bleeding from the intestinal tract occurred in 18 cases.

VOMITING. This, as an early symptom, was present in 22 cases, and was accompanied by colic in 19 of them. Haematemesis occurred in three cases, and in one, a girl aged 7 years, vomiting was so intractable that intravenous fluids were required for three days.

HAEMATURIA. Macroscopic haematuria occurred in 16 cases: in seven of these it was a presenting symptom and in nine it occurred after admission. In 27 cases in all, albumin, red cells, leucocytes and occasional casts were reported in the urine in one or more of the early specimens examined. Sixteen of the 27 patients had clear urine before they were discharged. Only one patient in this group was re-admitted and he relapsed with a severe, necrotic rash, but on this occasion there was no renal involvement. Of the remaining 11 cases, nine had urine which still contained albumin, red cells and casts on discharge. Two children (to whom reference has already been made) died from chronic nephritis and its complications.

Relapses and Re-admission. The tendency for patients with the Schönlein-Henoch syndrome to have a recurrence of their symptoms is well known, and 31 of our 59 patients had relapses while they were still in hospital. The causes are shown in Table 3. The commonest form of relapse was a recurrence of the rash, usually as an isolated phenomenon (nine cases) but also in association with haematuria (five cases), bleeding from the bowel (five cases) and abdominal colic (three cases).

TABLE 3
SYMPTOMS OF RELAPSE IN 30 CASES OF THE SCHÖNLEIN-HENOCH SYNDROME CASES ADMITTED TO ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL, 1943-1955

Recurrence of rash	9 cases
Rash and haematuria	5 ,,
Rash, colic and intestinal haemorrhage	5 ,,
Rash and colic	3 ,,
Rash and joint swelling	2 ,,
Haematuria	4 ,,
Colic and vomiting	3 ,,
Total :	31 ,,

A majority of the patients attended an out-patient clinic after discharge from hospital. Five patients reported recurrences of the rash and two had had severe abdominal colic.

Ten, six males and four females, of the 59 patients in this series were re-admitted to hospital. Nine were re-admitted within four months of their discharge and one boy returned after two years. He had a recurrence of haematuria, although in the two-year interval, during which time he attended the out-patient clinic, his urine had been clear. The haematuria was profuse and recurred on several occasions during his first week in hospital, but it was his only symptom on this occasion. Previously he had had purpura, haematuria, intestinal haemorrhage and colic. He was again discharged with normal urine and renal function tests.

Of the other nine patients who were re-admitted, three had purpura and six had haematuria; four of the latter have developed chronic nephritis.

Other Complications. It is interesting that chorea was associated in two cases. One child, who had been admitted with purpura and colic, developed chorea during the convalescent period of her illness. The other child had chorea first, and one month after recovery she developed purpura and joint swellings. She now has chronic nephritis.

Asthmatic attacks were recorded in one patient,

a boy of 13 years. He had had asthma in infancy but had been free from attacks during later childhood. An eosinophilia above 5% of the total white cell count was recorded in six cases, the figures ranging from 6 to 14%.

The Incidence of Renal Damage in Both Series

In the first series of 35 cases 19 had renal involvement at the time of their initial illness and four still had red blood cells and albumin on discharge.

The general follow-up has revealed that these four patients now have normal kidney function tests, but that renal damage has occurred in four other cases. Of the four atypical cases, three developed renal complications and two of these died, one having periarteritis and the other chronic nephritis and pericarditis. The third child had persistent albuminuria for six years but now appears to have recovered.

In the second series of 59 cases, 27 patients had abnormal urinary findings at some time. Two children died from chronic nephritis. Nine others left hospital with persistent albumin and red cells in the urine; all have been followed in the Outpatient Department and five have now been discharged. The four remaining children with initial renal involvement have all developed chronic nephritis.

During the follow-up investigation it has been discovered that one other child, who did not have any evidence of renal damage at the time of the acute illness five years ago, now has impaired renal function, as shown by urea clearance test and Addis count.

In reviewing the whole series of 94 patients it has been possible to carry out renal function tests in 34 cases. Of these 22 had some renal involvement at the time of their acute illness, and 12 had no urinary abnormality. Of those who had initial renal damage, seven now show impaired kidney function. Of those who had no renal damage in the first place two patients show evidence of renal deficiency and in both cases it is of moderate severity. It is also of interest that two other children, who have had albuminuria and recurrent haematuria, for eight and seven years respectively, are now clinically well and recent renal function tests show no abnormality.

Discussion

The view has been expressed that there has been an increasing incidence of the Schönlein-Henoch syndrome over the past several years. Certainly more cases are reported now than formerly. In the five years immediately before 1948 an average of 2·8 cases per annum were diagnosed at Alder Hey Children's Hospital. In 1948 the number more than doubled and, during the seven ensuing years, the average number of new cases has been 10·3 annually. Possibly this increase is ascribable in part to the interest aroused by Gairdner's valuable paper published in 1948. It is a matter for speculation whether there has been a real increase in the incidence of the syndrome, or whether awareness of the condition as a clinical entity has led to the recognition of more cases. The number of cases diagnosed at Alder Hey Children's Hospital during the past four years has remained fairly constant (Table 1).

There is general agreement that the greatest danger of the Schönlein-Henoch syndrome is renal damage. Evidence that renal damage occurred at some stage in the syndrome was found in 11 (42%) of 26 cases (Oliver and Barnett, 1955) and in 19 (47·5%) of 40 cases (Philpott, 1952) and in 46 (49·5%) of 94 cases in the present series. Such damage was shown by albuminuria, haematuria or both, but it has not been established that these findings constitute acute glomerulonephritis. When referring to the joint manifestations of the Schönlein-Henoch syndrome, Gairdner (1948) wrote that these were not in the least like rheumatism. Is it not equally true that the initial renal involvement is not in the least like nephritis? Neither facial oedema nor hypertension are commonly found, nitrogen retention is rare, and the erythrocyte sedimentation rate tends to settle to a normal level within a short time despite continued haematuria. Wedgwood and Janeway (1953) have recorded another important difference: serum complement is normal in the Schönlein-Henoch syndrome and is markedly reduced in true nephritis.

In the present series it has been noted that leucocytes are present in the urine in greater numbers than in most cases of acute nephritis. Here, then, is an atypical picture, which might be better described as 'renal bleeding' yet, as the present series shows, this earlier involvement is a pointer to the possibility that lasting renal damage may ensue.

Clark (1956), reviewing 265 children with nephritis, has commented upon the complex and infinitely variable pictures presented, and Rubin (1955), with reference to the Schönlein-Henoch syndrome, remarked upon the 'wide pattern' of renal involvement in this disease. A study of the patients who have had renal involvement in our own series confirms this. The clinical picture of subacute nephritis (with massive albuminuria, oedema, low plasma protein, reversed albumin/globulin ratio and high blood cholesterol) was seen as well as chronic nephritis with hypertension and uraemia.

Recurrences of the syndrome, especially with renal symptoms, have been considered detrimental to the ultimate prognosis, but this assumption has not always proved correct in our series. Two patients have had several recurrences and yet their renal function tests have become normal.

In the future some help in distinguishing the types of nephritis that occur may be forthcoming from a study of electrophoresis of the serum proteins. In one of our cases the pattern of distribution of serum protein fractions corresponds to that found in the Ellis type II nephritis. It is interesting that one other case, uncomplicated by renal damage, showed an electrophoretic pattern characteristic of the early phase of acute rheumatism. The authors hope to report the result of further investigations along these lines.

Summary

From 1943 to 1955, 94 examples of the Schönlein-Henoch syndrome have been admitted to Alder Hey Children's Hospital, Liverpool. The incidence of renal sequelae has been investigated.

During their initial illness 46 children had some renal involvement: two children died with chronic nephritis and 13 left hospital with persistent albumin and red cells in their urine. A recent follow-up with Addis counts and urea clearance tests show that nine of these 13 children now have no evidence of kidney disease; the remaining four have developed chronic nephritis. In this series, therefore, the incidence of chronic nephritis is approximately 6%.

In addition, it has been found that five other children, who did not have renal involvement at the time of their original illness and are now symptom-free, have some impairment of renal function as shown by Addis counts and urea clearance tests.

Four atypical cases described in a previous paper have been reviewed: two of these died.

Our thanks are due to Professor N. B. Capon for his helpful criticism and advice, to colleagues who kindly allowed us to include their cases in this series, and to Mr. J. Ireland for biochemical investigations.

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NEUROLOGICAL COMPLICATIONS IN THE SCHÖNLEIN-HENOCH SYNDROME

BY

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Although a few textbooks persist in describing separately 'Schönlein's purpura' and 'Henoch's purpura' the recognition of the Schönlein-Henoch syndrome as a disease entity cannot now be disputed. The characteristic exanthem, the frequent occurrence of arthritis and intestinal symptoms, together with the possibility of renal damage, are well known.

Serious neurological complications of this condition must be rare, judging from the medical literature, and therefore the following cases are of particular interest.

The diagnosis of the Schönlein-Henoch syndrome in each patient was based on the finding of an exanthem of the type and distribution described by Gairdner (1948), namely, intestinal colic and vomiting, arthralgia and nephritis (in two of the three cases).

Case Reports

Case 1. Howard M., born on February 19, 1947, was admitted to hospital on June 29, 1955, with abdominal pain, vomiting and passage of bloody stools. The following day laparatomy was performed. There were several areas of small gut showing extensive subserous haemorrhages, and the bowel lumen was filled with blood. After five days he developed typical exanthem and on the same day complained of severe headache. Later in the day he had a generalized convulsion, his blood pressure being 160/110 mm. Hg. The C.S.F. was normal. He was given hexamethonium to control hypertension, but this resulted in gut and bladder paralysis. The blood pressure subsequently settled spontaneously without further convulsions.

On July 8 he suddenly complained of intense headache. Examination revealed much spinal rigidity, and the C.S.F. was intimately bloodstained. The symptoms cleared in 10 days, during which the right wrist became swollen for two days, and he suffered several attacks of abdominal pain. The C.S.F. was found to be xanthochromic on July 19. On July 12 the urine became abnormal for the first time (protein and red cells present). No further skin eruptions occurred.

During August there was a deterioration in the patient's renal condition. Oedema and ascites appeared and the blood pressure again rose. On August 4 the blood pressure was 160/110 mm. Hg and next day there was some generalized twitching. Reserpine was used to control hypertension and was discontinued after a week. A trial with cortisone was started on August 15 but had to be discontinued after 48 hours owing to a dramatic increase in the oedema. The oedema disappeared equally dramatically on discontinuing hormone treatment.

The boy remained fairly well, but rather wasted, and with abnormal urine. On September 11 he suffered a mild convulsion (blood pressure 140/110 mm. Hg) and developed left hemiplegia, which has persisted. Since this time there has been a progressive improvement in his general condition. The urine remains abnormal with protein 20-100 mg. %, and a few red cells and granular casts are present. The blood pressure remains normal (90/60 mm. Hg). With physiotherapy there has been some improvement in the hemiplegia, but he is still in hospital.

This case illustrates (1) convulsions, presumably hypertensive, in the absence at first of urinary abnormalities; (2) subarachnoid haemorrhage; and (3) intracerebral haemorrhage or thrombosis, presumably due to arteriolitis.

Case 2. Sheila N. was born on June 14, 1939.

She was admitted to hospital on October 16, 1949, with abdominal pain and vomiting. She had had a haemolytic streptococcal throat infection two weeks previously.

Appendicitis was suspected but on October 18 at laparotomy a normal appendix was removed. Three enlarged ileocaecal glands were noted.

The exanthem of the Schönlein-Henoch syndrome appeared over the buttocks and left forearm on October 20, and the patient complained of arthralgia with periarticular oedema.

Melaena and further crops of the exanthem appeared during the next few days, but the discomfort diminished.

On November 4 she complained of frontal headache and she became confused. Her blood pressure was 150/90 mm. Hg. Her symptoms were worse by the following day and neck stiffness was noted. Lumbar puncture revealed heavily bloodstained fluid under con-

siderable pressure. Subarachnoid haemorrhage was diagnosed and was treated conservatively.

The cerebral symptoms cleared rapidly during the next day or two, but on November 7, 1949, a trace of albumin and a few red blood cells were discovered in the urine.

During November and December the patient complained of occasional intestinal colic and arthralgia, and there was deterioration in the renal condition, marked by many fluctuations in the albumin and red blood cell content of the urine. Hyaline and granular casts were prevalent.

Early in February her urine contained 7 g. per litre of albumin. She became very oedematous early in March, and died on March 14, 1950.

A necropsy limited to the abdominal cavity was allowed. The findings were subacute nephritis with preglomerular arteriolitis in some areas of the renal cortex.

This case illustrates (1) subarachnoid haemorrhage and (2) renal failure and death.

Case 3. Caroline A. was born on April 22, 1949.

She was first seen at home on October 29, 1955. Two weeks previously she had a mild sore throat lasting two days. Five days previously she became listless and vomited once the following day. A day later she complained of pains in several joints, but no swelling was noticed. The day before being seen she developed a rash on the arms, legs and buttocks. The Schönlein-Henoch syndrome was diagnosed and the case was left to the care of the family physician. The next day severe abdominal pain developed, and dark fluid stools were passed for three days. On November 1 she complained of a 'funny feeling', her expression became vacant and later she lapsed into unconsciousness but did not convulse. After one and a half hours she awoke and was rational. Two hours later a similar episode occurred, and after another two hours a third episode, in which she had a major convulsion lasting 10-15 minutes. Subsequently she was admitted to hospital on the same day.

On admission the blood pressure was 130/80 mm. Hg. Treatment with phenoxymethyl penicillin and phenobarbitone was given. A further generalized convulsion occurred on the day after admission. This was rapidly controlled with intramuscular paraldehyde. She continued to have crops of skin lesions and occasional attacks of abdominal pain, with bloody stools. The blood pressure began slowly to settle, but on November 18 it rose suddenly to 145/120 mm. Hg. She had a further convulsion which was promptly controlled with intramuscular paraldehyde. Subsequently the blood pressure gradually subsided without specific treatment. On December 8 the blood pressure was 90/40 mm. Hg and only slight fluctuations were encountered subsequently.

In view of the continued skin and abdominal features, treatment with prednisone was begun on November 11, but this had no dramatic effect on the course of the disease. Between December 6 and 13 the drug was gradually withdrawn. After December 16 no further skin eruptions or attacks of abdominal pain occurred. On December 17 she was discharged for further surveillance at home. During the first two weeks at home she had several mild attacks of abdominal pain, but her stools remained normal and there was no further exanthem. Her blood pressure remained steady. After a further week she was allowed up and has remained well ever since.

At no time during the course of the illness or subsequently has any abnormality in the urine been detected, and the blood urea has been normal.

This case illustrates convulsions, probably hypertensive in origin, in the absence of urinary abnormality.

Discussion

Little mention of involvement of the central nervous system can be found in the literature dealing with the Schönlein-Henoch syndrome. Osler (1914) in the last of his four articles on the visceral lesions of purpuras and allied conditions described neurological complications, but only one case undoubtedly suffered from the Schönlein-Henoch syndrome. This patient, a 13-year-old boy, had nephritis as well as intestinal colic and the exanthem, and had a transient hemiplegia on several occasions. Gracie (1924) described the case of a 13-year-old boy who suffered from colic, arthralgia, exanthem and macroscopic haematuria. The child had several convulsions but later appeared to make a full recovery. Other cases of convulsions have been mentioned in connexion with this disease, but they have all had nephritic features (Levitt and Burbank, 1953; Wedgwood and Klaus, 1955). Case 3 reported above had no signs of renal involvement at the time of the convulsions.

Green (1946) described a girl aged 7 years who suffered from a subarachnoid haemorrhage during the course of an attack of the Schönlein-Henoch syndrome. This would appear to be the only previous recording of such a complication, although he quoted a personal communication from Davis who claimed to have seen two similar cases in 1,100 (adults and children) studied by him. Davis (1948), however, makes no mention of these in his own paper.

That the disease process is essentially an arteriolitis was made plain by Gairdner (1948). The skin is invariably affected and the gut and joints are frequently involved. It is not certain what lesion is present in the kidneys, which are diseased in a large number of cases (Philpott, 1952). The course and prognosis of the kidney lesions suggests something different from glomerulonephritis, probably the same arteriolitis which involves the skin and gut. Widespread arteriolitis and arteritis have been

described in necropsy reports by Wassilieff (1937), Gairdner (1948) and Levitt and Burbank (1953). It would be surprising if the cerebral vessels escaped and the cases recorded in this paper strongly suggest that they are involved. Headache was noted in 25% of 116 cases of the Schönlein-Henoch syndrome (Lewis, 1956). By no means all these patients with headache had either hypertension, fever or nephritic features, and it seems likely that the symptom is due to the same vascular changes as found in the skin and elsewhere.

The convulsions suffered by Cases 1 and 3 were presumably hypertensive in origin, although they may have resulted directly from arteriolitis in the cerebrum. Case 3 is particularly interesting in that her urine never became abnormal. (Addis counts, however, were not performed in this case.) It must remain a matter of speculation as to whether she had preglomerular arteriolitis or not.

Summary

The cases of two children who developed subarachnoid haemorrhage during the course of an attack of the Schönlein-Henoch syndrome are described, together with a report of a case of hypertensive encephalopathy in the same condition without, however, renal abnormality.

The literature is discussed.

We wish to thank Professor R. W. B. Ellis for his helpful advice and for allowing us to publish Case 2.

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ABERDEEN GROWTH STUDY

I. THE PREDICTION OF ADULT BODY MEASUREMENTS FROM MEASUREMENTS TAKEN EACH YEAR FROM BIRTH TO 5 YEARS

BY

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Between 1923 and 1927 the late Professor Alexander Low measured a series of newborn babies, and in the subsequent years he succeeded in measuring 65 of the boys and 59 of the girls at each birthday up to and including 5 years. Twenty-one physical measurements were made on each child (always by Professor Low himself) and a record was kept of the number of erupted teeth, the time of closure of the anterior fontanelle, the age and parity of the mother, the age of the father and whether the baby was breast or bottle fed. The complete raw data of this growth study were published posthumously a few years ago (Low, 1952).

There is very little information available on the relation between growth in the first five years and adult size and shape, and it occurred to us that the value of this growth study, which was the first longitudinal one made in Great Britain, would be greatly increased if we could find and remeasure some of the subjects now that they were grown up. Accordingly a search for them was instituted, and all except six were successfully traced. Not all, however, were available for measurement, and of those that were, a few could not be persuaded to make what, in many cases, was an arduous journey from their homes to Aberdeen or to London. In all we managed to measure, photograph and somatotype exactly 65% of the original group of both men and women. Thus our records, made between 20 and 25 years after the subjects' last attendances with Professor Low, concern 42 men and 38 women.

The details of the follow-up are given in Table 1. A quite surprising number of subjects had died, all except one from natural causes. One of the men was crippled with rheumatoid arthritis, and another was a leucotomized schizophrenic. None of the women were ill, but two were more than six months pregnant, and so were excluded. Six of the 38 women measured were also pregnant, but their pregnancies had lasted less than six months and they have been included in the statistics below without any alteration in their records; their weight and probably their fat measurements are slightly elevated, but their skeletal ones should be unchanged. (All the various statistics given in the section on results below have been also calculated for weight with these six women excluded, and none of them differed sensibly from the figures given here for the total 38.)

TABLE 1
FOLLOW-UP OF ABERDEEN GROWTH STUDY SUBJECTS AFTER 20 TO 25 YEARS

	Men	Women
Remeasured	42 (65%)	38 (65%)
Died	6	5
Emigrated	8	3
Sick or > 6 months pregnant	2	2
Untraced	3	3
Refused attendance ..	4	8
Total .. .	65	59

The great majority of the adult measurements were done at Aberdeen in January, 1953, the remainder in London during the subsequent three months. All subjects had the original measurements repeated, using the same technique as Professor Low, and in addition had subcutaneous fat and bicondylar measurements taken, together with standardized nude photographs for photogrammetric anthropometry and somatotyping (Tanner, 1955, appendix). In this first paper we are concerned with the prediction of adult measurements from childhood ones, and to this end give the means and standard deviations at each age of supine length, weight, head length and breadth, shoulder and hip widths, and length of lower arm and foot. These dimensions were chosen so that most of the various factors described in adult physique and reflecting differential growth were represented (see Tanner, 1953).

The inter-correlations between measurements at each year are given for each dimension, and also the cumulative percentages of the adult variance explained by multiple regressions using all measurements up to 0, 1, 2, 3, 4 and 5 years respectively.

In subsequent papers we expect to discuss (*a*) the fitting of equations to the individual growth curves and the relations between distance, velocity and acceleration in individuals; (*b*) the relations between the various dimensions at various ages, that is, change of shape with age; (*c*) the assessment of developmental maturity from growth curves; and (*d*) the relation of adult somatotype to the pattern of growth.

Results

Before the statistics given below were calculated the childhood data were carefully examined for errors of measurement and recording, such as are known to occur in even the best regulated studies (Healy, 1952). Graduating curves of the form $y = a + bt + c \log (t + \frac{3}{4})$, where y is the measurement recorded at t years, were fitted to each individual's data for each measurement and the residuals (recorded figure minus predicted figure) at each age examined. In this way some clearly erroneous recorded figures were discovered and altered (usually by 10 units) to the presumed proper value. A list of these alterations is given in the Appendix; suffice it here to say that we have altered a figure only when we were quite satisfied that an error had occurred. The total number of alterations were: weight, nil; head length, 1; head breadth, 1; stature, 14; biacromial width, 4; bitrochanteric width, 10; foot length, 3; cubit (forearm plus hand length), 9. The total corrections are 42 out of 3,360 linear measurements, that is 1·2%, which is not unreasonable in the light of other workers' experience in this field (Healy, 1952). The uneven distribution of these alterations between different measurements is partly due to the fact that some measurements are less prone to gross errors of reading the instruments than others, and partly to the genuine measuring errors in certain measurements, e.g., shoulder width, being sufficiently large to make the detection of gross errors somewhat uncertain; undoubtedly in this latter class of measurements, and in weight, a few undetected gross errors remain.

The means and standard deviations for each measurement at each year are given in Table 2.

TABLE 2
MEANS AND STANDARD DEVIATIONS AT EACH AGE FOR 42 MALES AND 38 FEMALES

		Age in Years						
		0	1	2	3	4	5	(Adult) 25-30
Supine length*†	male	495·4	733·3	839·4	920·8	991·8	1,048·1	1,719·2
		15·83	30·41	38·40	41·20	40·94	43·77	64·90
	female	497·3	725·9	838·1	921·8	997·8	1,058·8	1,611·7
		18·27	28·84	36·63	34·44	41·12	45·04	56·84
Cubit	male	136·5	188·0	216·2	236·2	254·5	268·7	460·3
		4·71	11·58	12·01	11·47	13·15	13·99	18·04
	female	136·7	185·6	213·4	234·7	252·9	268·3	418·5
		4·40	9·01	10·34	11·43	14·34	14·25	16·48
Foot length	male	79·2	110·6	125·7	137·1	148·0	155·3	251·7
		4·23	6·68	7·40	8·19	9·59	9·28	11·42
	female	78·8	108·6	123·8	136·0	147·1	156·2	229·9
		4·31	6·55	6·80	7·83	8·74	8·31	10·49
Biacromial	male	121·8	173·9	194·1	207·4	220·3	231·9	399·1
		4·50	11·80	12·54	11·26	11·58	13·83	15·69
	female	122·0	174·1	192·8	208·1	219·5	231·9	360·3
		5·02	10·23	9·49	10·82	11·96	11·10	13·60
Bitrochanteric	male	96·7	142·7	160·6	172·6	177·7	181·8	316·7
		3·96	7·86	8·12	6·46	6·63	7·00	14·09
	female	96·6	141·4	159·7	169·6	176·1	182·2	314·6
		4·46	7·81	7·53	6·39	6·78	6·93	16·66
Weight (lb.)	male	6·89	20·49	25·11	28·66	32·85	36·42	139·06
		0·97	2·52	2·23	2·37	3·39	3·40	14·46
	female	7·05	19·89	24·32	28·85	32·42	36·09	123·94
		1·01	2·21	2·00	3·19	4·09	4·13	19·57
Head length	male	119·4	160·1	168·9	172·4	175·0	177·0	192·3
		3·88	5·08	4·77	4·92	4·79	5·11	5·58
	female	120·0	158·0	165·4	170·5	172·4	174·4	184·1
		3·86	6·50	5·20	5·74	5·33	5·53	5·75
Head breadth	male	94·4	127·3	133·1	136·4	138·4	139·9	150·4
		4·19	3·91	4·69	4·46	4·17	4·48	5·54
	female	94·7	126·7	131·9	135·4	137·4	138·6	144·8
		2·53	4·11	3·82	3·99	3·96	3·89	4·21

* See text. † All measurements except weight in mm.

The data constitute a pure longitudinal series (Tanner, 1951), every child having been present at every age. Supine length in the table and throughout this paper refers to total body length taken with the child lying on its back: from age 0 to 3 length was measured this way, while at 4 and 5 and adulthood it was measured with the subject standing. The standing figures have been converted to supine ones by means of Palmer's (1932) table. A reliable conversion to standing height could not be made from these tables at the younger ages.

The mean values in Table 2 will be examined more fully in a subsequent paper, and call for little comment here. Up to and including age 5 there is very little if any sex difference in size; the adult sex difference comes about through the greater adolescent spurt of the male (Tanner, 1955). With regard to the standard deviations, it is especially noticeable that the figures at birth are much lower than subsequent ones. This is particularly true for biacromial and bitrochanteric diameters, and least marked for foot length and the head measurements. This low variability at birth is not a feature of any of the other published series of data covering this age range, in which the birth or shortly-after-birth standard deviations are usually only slightly less than the 1-year-old figures. It cannot be accounted for by the selection of children with unduly similar measurements since the standard deviations in the present series agree well with those for the much larger series of 900 children from which the individuals repeatedly measured were drawn (Low, 1950). This larger series seems to have been drawn from hospital cases without selection, except for the rejection of babies weighing less than 5½ lb. at birth. The possibility has to be entertained, therefore, that there was a tendency for the measurer to get oversimilar answers from one child to another when measuring 3-day-olds. Apart from this, the standard deviations in general increase slightly as the means increase, a familiar tendency in growth data. The high standard deviations at age 2 and 3 for bitrochanteric diameter may perhaps reflect the greater amount of fat over the hips at these ages.

In Tables 3A-H the correlations between measurements at different ages are presented. These tables are most simply examined in two parts: the correlations at ages 1-5, and those involving the adult measurements.

We will consider first the 1-5 block. There are several tendencies which might be expected *a priori*. First, correlations between years close to each other would be expected to be greater than correlations between years further apart. In other words, we

TABLE 3A

CORRELATIONS OF MEASUREMENTS AT SUCCESSIVE AGES

	0	1	2	3	4	5
Supine length, male						
0						
1	0·64					
2	0·48	0·85				
3	0·52	0·81	0·93			
4	0·46	0·78	0·88	0·93		
5	0·43	0·74	0·83	0·87	0·95	
Adult	0·25	0·65	0·79	0·80	0·81	0·77
Supine length, female						
0						
1	0·39					
2	0·41	0·76				
3	0·36	0·78	0·81			
4	0·40	0·78	0·82	0·90		
5	0·34	0·76	0·82	0·88	0·95	
Adult	0·29	0·70	0·74	0·78	0·82	0·81

TABLE 3B

	0	1	2	3	4	5
Cubit, male						
0						
1	0·35					
2	0·25	0·85				
3	0·37	0·78	0·87			
4	0·32	0·71	0·81	0·91		
5	0·33	0·72	0·82	0·88	0·92	
Adult	0·26	0·43	0·54	0·62	0·58	0·58
Cubit, female						
0						
1	0·15					
2	0·14	0·75				
3	0·14	0·65	0·86			
4	0·12	0·75	0·87	0·93		
5	0·11	0·69	0·80	0·90	0·92	
Adult	0·23	0·55	0·73	0·78	0·80	0·76

TABLE 3C

	0	1	2	3	4	5
Foot length, male						
0						
1	0·54					
2	0·50	0·83				
3	0·58	0·77	0·83			
4	0·49	0·64	0·72	0·87		
5	0·45	0·55	0·63	0·77	0·91	
Adult	0·37	0·54	0·60	0·65	0·54	0·46
Foot length, female						
0						
1	0·22					
2	0·28	0·81				
3	0·21	0·72	0·84			
4	0·13	0·59	0·68	0·85		
5	0·12	0·55	0·55	0·75	0·87	
Adult	0·48	0·68	0·59	0·64	0·60	0·54

TABLE 3D

	0	1	2	3	4	5
Biacromial, male						
0						
1	0·27					
2	0·30	0·74				
3	0·31	0·58	0·68			
4	0·28	0·35	0·41	0·75		
5	0·23	0·14	0·22	0·51	0·87	
Adult	0·12	0·43	0·33	0·37	0·13	0·00
Biacromial, female						
0						
1	−0·24					
2	−0·01	0·48				
3	0·19	0·10	0·44			
4	0·23	0·12	0·35	0·81		
5	0·12	0·09	0·41	0·59	0·84	
Adult	0·24	0·28	0·39	0·30	0·36	0·37

TABLE 3E

	0	1	2	3	4	5
Bitrochanteric, male						
0						
1	0·31					
2	0·46	0·62				
3	0·44	0·52	0·71			
4	0·30	0·31	0·46	0·82		
5	0·23	0·25	0·37	0·69	0·95	
Adult	0·28	0·25	0·49	0·45	0·36	0·36
Bitrochanteric, female						
0						
1	−0·09					
2	−0·06	0·61				
3	0·08	0·42	0·61			
4	0·06	0·39	0·50	0·77		
5	0·07	0·33	0·35	0·54	0·91	
Adult	0·17	0·52	0·52	0·43	0·40	0·32

TABLE 3F

	0	1	2	3	4	5
Weight, male						
0						
1	0·48					
2	0·43	0·83				
3	0·49	0·64	0·86			
4	0·51	0·66	0·72	0·84		
5	0·37	0·65	0·76	0·81	0·92	
Adult	0·38	0·57	0·51	0·57	0·55	0·59
Weight, female						
0						
1	0·03					
2	0·16	0·79				
3	0·17	0·70	0·64			
4	0·22	0·76	0·71	0·86		
5	0·16	0·76	0·72	0·85	0·94	
Adult	0·42	0·29	0·43	0·34	0·46	0·46

TABLE 3G

	0	1	2	3	4	5
Head breadth, male						
0						
1	0·35					
2	0·20	0·85				
3	0·31	0·85	0·91			
4	0·34	0·76	0·82	0·88		
5	0·38	0·77	0·80	0·88	0·97	
Adult	0·36	0·61	0·61	0·73	0·85	0·85
Head breadth, female						
0						
1	0·23					
2	0·09	0·85				
3	0·16	0·83	0·92			
4	0·26	0·82	0·88	0·92		
5	0·17	0·78	0·87	0·90	0·96	
Adult	0·14	0·66	0·77	0·75	0·81	0·79

TABLE 3H

	0	1	2	3	4	5
Head length, male						
0						
1	0·29					
2	0·20	0·79				
3	0·24	0·73	0·92			
4	0·29	0·80	0·86	0·88		
5	0·27	0·76	0·85	0·87	0·96	
Adult	0·10	0·62	0·59	0·56	0·71	0·75
Head length, female						
0						
1	0·32					
2	0·36	0·77				
3	0·35	0·69	0·81			
4	0·35	0·74	0·84	0·93		
5	0·40	0·72	0·79	0·93	0·96	
Adult	0·37	0·68	0·62	0·79	0·82	0·82

expect that in each column of the tables the coefficients will get less as the eye follows the column downwards, and in each row of the tables the coefficients will get more as we read from left to right; the highest figure in each column or row should be the one next to the diagonal line. In general this expectation is borne out. There are a few individual exceptions, probably due to the combined effects of measuring errors and genuine vagaries in the individual growth curves on account of illness or other causes. One thing, however, is very noticeable; all the birth correlations are at a considerably lower level than later figures, and they are also less regular. Thus, for the cubit measurements, for example (Table 3B), birth correlations are of the order 0·10 to 0·35, whereas all 1-year-old and subsequent correlations are over 0·65.

It is further to be expected that the correlations between adjacent pairs of years will get larger as the children get older and the growth rate slows down. This happens, as can be seen by following down the figures next to the diagonal line. The 1-2 year correlations average 0·76, the 2-3 year average 0·79, the 3-4 year 0·87, and the 4-5 year 0·93. The birth-1 year correlations, however, are all much lower, and average 0·27. Evidently birth measurements are very much less of a guide to future developments than are measurements taken at 1 year of age. Possible reasons for this are discussed below.

Examining now the adult correlations in Tables 3A-H, that is the lowest rows of figures, we see the same sort of effect. The pattern of these correlations can be most easily seen from Fig. 1 where the data for supine length, head breadth, cubit, foot length, weight, biacromial and bitrochanteric diameters are graphed, with male and female correlations averaged. Consider first supine length, the top line: there is a steep rise in adult correlation from birth to 1 year and a lesser but distinct rise from 1 to 2. After this the rise becomes quite small and the adult/5-year correlation is actually slightly below the adult/4-year correlation. All measurements except body weight show this steep rise in adult predictability from birth to 2 years. Weight does show a rise, but it is only from 0·40 to 0·53. This simply confirms what we have already noticed; that measurements at birth are a singularly worse guide to future development than measurements taken a few years later.

The other striking feature of Fig. 1, however, is certainly less expected. Instead of the curves continuing their parabolic upward course to age 5, all except weight and the two head measurements show a stationary or downward trend after age 3. In other words, we can better predict most adult

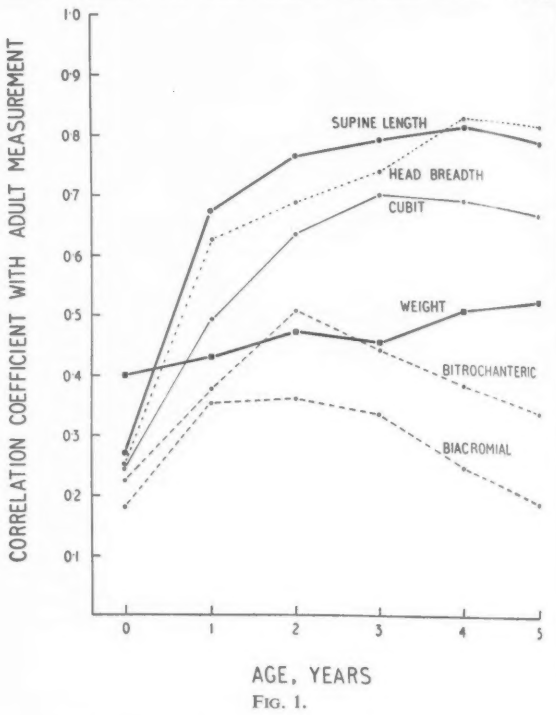

FIG. 1.

dimensions from measurements taken at age 3 than from measurements taken at age 5. This is particularly true of the two body breadth measurements where the adult/5-year correlations are very small indeed. There is further discussion of this below.

TABLE 4
PERCENTAGE OF ADULT VARIANCE ACCOUNTED FOR BY MEASUREMENTS AT PREVIOUS AGES

Measurements available at ages		0	0, 1	0, 1, 2	0, 1, 2, 3	0, 1, 2, 3, 4	0, 1, 2, 3, 4, 5
Supine length	male	4	43	62	67	68	67
	female	6	46	56	61	65	64
Cubit	male	4	16	26	34	32	30
	female	3	31	51	59	63	62
Foot length	male	12	26	32	37	35	34
	female	21	55	54	59	60	59
Biacromial	male	0	15	12	13	14	12
	female	3	13	18	16	17	15
Bitrochanteric	male	6	8	22	23	22	25
	female	0	27	32	31	30	27
Weight	male	12	30	29	37	35	42
	female	15	21	25	23	26	25
Head length	male	0	36	37	36	48	56
	female	11	46	46	65	70	69
Head breadth	male	11	37	40	53	72	72
	female	0	40	57	56	64	63

The question arises whether the prediction of the adult dimension would be much better if in addition to the record at age 5, say, we also had available all the previous information about the child's growth, that is the records at 0, 1, 2, 3 and 4 years. In Table 4 this question is answered for the present data. The figures given are the percentages of the adult variance of each measurement accounted for by regression on the measurement at birth, then birth and 1 year combined, then 0, 1 and 2 years, and so on up to the last column of the table, where the percentage of adult variance explained by all the information we have available is given. (The 'percentage variance explained' will be recognized as analogous to the square of the multiple correlation coefficient, but is preferable to the latter because, unlike R^2, it allows for the effect of decreasing degrees of freedom in the estimate of error as the number of independent variates gets larger. Thus it is possible for the percentage variance explained actually to decrease slightly as additional variates are added in, if they contribute little or nothing to the prediction.)

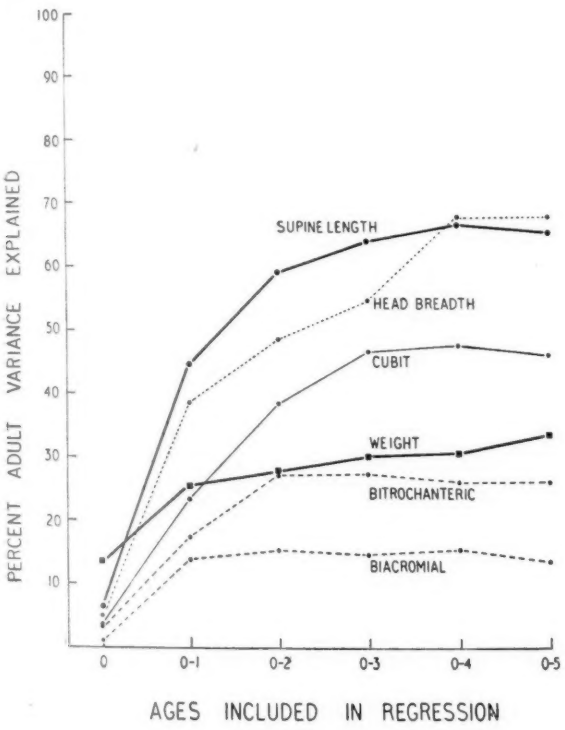

FIG. 2.

The general pattern of the figures in Table 4 can be seen plotted in Fig. 2, where the male and female figures have been averaged. The curves resemble closely those of the ordinary adult correlations given in Fig. 1, except, of course, that the drop after 3 years in the simple correlations is flattened into approximately a horizontal line in the multiples. The same conclusions appear, however. Predictability of adult dimensions is practically nil at birth, increases fairly sharply for most dimensions to 2 years, slightly more to 3, and thereafter fails to improve. The straight correlations showed that knowing the 4- or 5-year measurement is no better, and in some cases is worse, for prediction than knowing the 2- or 3-year-old measurement. These further multiple regression figures demonstrate in addition that if one does know the 3-year-old measurement practically no further information is obtained by taking measurements at 4 and 5 years of age. In other words, the rate of growth between ages 3 and 5 is apparently without predictive value for adult dimensions. Actually the rate of growth as such is of very little predictive value throughout, because the multiple regressions at age 3 (which embody rate of growth from 0 to 3 as well as actual size at age 3) are very little better at predicting adult size than is the simple regression on size at 3 years. In supine length, for example, the percentage of adult variance explained by the measurements at 0, 1, 2 and 3 combined is (Table 4) 67% for males and 61% for females, whereas the percentage adult variance explained by supine length at age 3 alone (from Table 3A) is 64% for males and 61% for females. This point will be elaborated in a later paper.

Discussion

Low Birth Correlations. Amongst the possible causes of the low birth correlations are the following:

LARGER MEASURING ERRORS AT BIRTH THAN SUBSEQUENTLY. This is possible but unlikely; the experience of most anthropometrists is that the difficult age for measuring children is not at birth but between $1\frac{1}{2}$ and 2 years when the child is old enough to protest but not mature enough to cooperate. In any case no reasonable amount of unreliability of measurement could have lowered the correlations to the extent found.

MATERNAL MALNUTRITION DURING PREGNANCY. The mothers were mostly drawn from a working class group in the days before antenatal care services were well developed. It is likely that some ate a good deal less than the optimal diet during pregnancy, and the effect of this could be to throw some of the foetuses off their (presumably) genetically-determined curves. There is one fact which stands out clearly against this explanation, however: in the Brush Foundation study (Simmons, 1944) at Western Reserve, Cleveland, the same tendency of

the birth correlations is seen. The correlations between birth weight and weight at 1 year were 0·32 and 0·49 (boys and girls), whereas subsequent adjacent-year correlations are 0·85 for 1-2 years and over 0·90 thereafter. For height the birth-1 year correlations were 0·40 and 0·30; 3 months-1 year correlations were 0·68 and 0·75, and 1-2 year correlations 0·88 and 0·84. These mothers and children were all drawn from the highest economic groups of American life and their diet must have been very nearly optimal. Again, the study of Bayley and Davis (1935) on Californian children shows the same depression of the 1-month-old correlations for the several measurements that they report from 1 month to 3 years. This group, too, is at least a well-nourished one, and their correlations are very similar to ours. For example, the 1-month correlations for hip width (sexes combined) with 1, 2 and 3 years are 0·37, 0·32 and 0·23, whereas the 1 year-2 year correlation is 0·80. For weight the 1 month-2 year correlation is 0·45, the 1 year-2 year correlation 0·91.

MATERNAL ENVIRONMENT, GENERAL AND LOCAL. This would seem to be the most acceptable explanation. Both in animals and man the birth weight is to a considerable extent dependent on the prenatal environment. Thus, in man the inborn growth rate of the foetus is modified during the last two months or so of pregnancy by maternal factors which are quite distinct from the maternal genes influencing the child's ultimate size. These factors affect not only the rate of prenatal growth, but also the gestation time. They appear to be both systemic and uterine, and they serve to hold back in growth, and also to expel early, the genetically large child who happens to be developing in a small-sized mother (McKeown and Record, 1952, 1953). The mother's environment and nutrition play a part in these prenatal influences, but apparently not a more important one than her heredity (Robson, 1955), which presumably acts through hormonal constitution and uterine and placental size. The effect of this prenatal influence does not, however, persist. Cawley, McKeown and Record (1954), for example, have shown that, although the correlations between gestation time and birth weight and birth length are about 0·35 and 0·31 (even when heights of father and mother, maternal age and birth rank are allowed for), the correlations between gestation time and 1-year-old weight and length are practically zero. Unfortunately we have no data on the gestation time of our Aberdeen subjects. Conversely, the correlation with average parental weight in the Oxford Child Health Survey children was only 0·22 at birth, but rose to 0·42 by age 1 (Hewitt and Stewart, 1952).

We are thus presented with a picture of, presumably, a genetically determined growth curve which in favourable environmental circumstances the child may follow at first in the uterus and later outside it. But towards the end of his uterine existence he may be deflected very considerably from this curve by the characteristics (both genetical and environmental) of his mother, and after birth he takes a little time to get back on to it, somewhat after the manner of a growing animal who has passed through a period of not too severe malnutrition (see Tanner, 1955, p. 85). There is, indeed, a negative correlation between birth weight and weight gain during the first six months (Thomson, 1955) and, to a much smaller extent, during the second six months (Norval, Kennedy and Berkson, 1951) which probably reflects this catching-up mechanism. The same applies to birth length and length increment (Simmons and Todd, 1938). This is probably still an over-simplified picture. We cannot be sure that the vagaries of intra-uterine life may not sometimes produce a permanent effect, though comparison of identical and non-identical twins makes this appear rather unlikely. In any case it looks as though prediction of a child's ultimate adult size from his size at birth is at present a losing game; by 1 year one has at least something to go on, and by 3 years quite a good deal. This does not necessarily mean that adult shape cannot be predicted from shape at birth or that it can be predicted from shape at, say, 3 years; the problem of 'guessing the somatotype' remains entirely open. We are now in process of examining the constancy during growth of various combinations of measurements, and hope to report on this later.

It is interesting that the largest correlation between an adult measurement and a birth measurement is that for weight. This extends the data of Illingworth and others (Illingworth, Harvey and Gin, 1949) who showed that heavier babies on the whole turned into heavier children. The prediction equations of weight at age 25-30 from birth weight in the present data are

Adult weight (lb.) = 5·62 birth weight (lb.) + 100·3 (men)
Adult weight (lb.) = 8·06 birth weight (lb.) + 67·2 (women)

with the large standard errors of prediction of ±13·4 lb. for men and ±17·8 lb. for women. For the prediction of adult weight from 5-year-old weight the regression coefficients are 2·50 and 2·16 for men and women respectively, with standard errors of prediction of 11·7 lb. and 17·4 lb.

Diminution of Correlations at Ages 4 and 5. The diminution of adult correlations after about age 3 for all measurements except weight and head length

and breadth (see Fig. 1 and Table 4) seems to admit of two possible explanations.

PERIODS OF ACCELERATION. Some sort of acceleration may be occurring on the curves from 3 onwards, with its beginning falling at different ages in different individuals. This happens, as is well known, at adolescence and it has precisely the effect of lowering the correlations with adult measurements during the years of the spurt, so that, for example, one can predict the adult height better from height at age 12 than at age 14 (see Tanner, 1951, 1955, p. 65). But there is no other evidence known to us that any period of acceleration does occur at the 3-5 years of age period. This matter needs further examination.

EFFECT OF MALNUTRITION. The children reached this age at near the height of the 1928-30 depression and it is probable that some suffered real privation. Nevertheless, if differential degrees of malnutrition have lowered adult prediction for shoulder and hip width, it is hard to see why they have not done so for weight.

Neither of these explanations seems to us very satisfactory and more research needs to be done, with children followed during their whole course of growth. In the literature there are a few records of correlations of near-adult height and weight with previous measurements from age 7 onwards (summarized in Fig. 1 of Tanner, 1951) and it looks as if the stature correlation curve given in Fig. 1 can be continued slowly upwards to reach about 0·84 at ages 10-12, after which it falls again till after adolescence. The weight curve probably also rises continuously to somewhere around 0·7 before adolescence, though this is less certain.

Sex and Measurement Differences. There are some sex differences apparent in the figures of Tables 3 and 4, and also and much more strikingly some differences between body measurements. None of the sex differences is very large, but perhaps the consistently lower predictability of cubit, foot length and head length in the male calls for some comment. A reason why *all* male predictions should be lower than female ones comes readily to mind. The adolescent spurt is of greater magnitude and almost certainly of greater variability in the male. (Thus the standard deviations of height, for example, are practically the same for boys and girls before puberty, but some 8% greater for boys after puberty.) If the magnitude of the spurt is relatively independent of the course of growth before adolescence, which on present evidence seems likely, then the predictability of adult male values should be lower. The curious thing, however, is that for supine length the predictabilities of male and female are almost identical. So, although this explanation may be true, more work needs to be done before the situation becomes clear. In particular, it would be very interesting to know how closely the immediately pre-adolescent dimensions of boys and girls could be predicted from earlier measurements. It is a great pity that our measurements do not continue till age 11 or 12.

There are considerable differences in predictability between different body measurements. Supine length has the highest predictability of those we have studied, which is a fortunate practical accident, as this is what people most usually want predicted. The regressions of adult supine length on length at age 3 are

$$\text{Adult length (mm.)} = 1{\cdot}27\ (\text{length at age 3, mm.}) + 549\ (\text{men})$$
$$\text{Adult length (mm.)} = 1{\cdot}29\ (\text{length at age 3, mm.}) + 423\ (\text{women})$$

with standard errors of estimate of 39 and 36 mm. (For conversion to adult standing height subtract about 15 mm.) However, the reader should be warned that because of the secular trend to a greater amount of growth completed at a given chronological age (see Tanner, 1955, p. 88) these figures will probably give too high predictions if applied to present-day children. It is interesting that Bayley and Pinneau (1952) give the percentage of adult stature achieved at age 3·0 as 53·5% for boys and 57·2% for girls: these figures are for Californian children studied about five years later than the Aberdeen ones. For the Aberdeen children the figures are almost identical: 53·6% and 57·2%.

Next to supine length in predictability came the head measurements, which are the only ones which show a substantial betterment in prediction from 3 to 5. It is astonishing that despite the relatively small amount of growth still to occur after age 5 the prediction of adult head size is relatively less accurate than that for supine length.

Body breadths have much the lowest predictability, for reasons that are not at present clear. Biacromial diameter is admittedly very difficult to measure in young children, and the correlations may be lowered by a good deal of measuring error. Bitrochanteric diameter, however, is fairly straightforward, though affected to some extent by fat. However, neither explanation seems sufficient to account for the very low values obtained and the question must be raised (though we certainly cannot answer it) as to whether these breadth dimensions are more affected by environmental circumstances than are the lengths. It is very necessary that this material be checked with the other growth data

available in a few places in the United States and gradually becoming available in the United Kingdom.

Weight stands in between the lengths and breadths. The correlation between adult and birth figures is greater for weight than for any other dimension, but at later ages it rises rather less than for most others. (The true birth weight correlations might well be slightly higher than those given here, because these are for weight at 3 days post-partum, which unfortunately is at the peak of the post-partum weight loss. As different babies reach their maximum loss on different days (Meredith and Brown, 1939) a small extra source of variability affects these figures.) As in the case of the other measurements, the predictability of adult weight from weight reached at 5 years can be scarcely at all improved by knowledge of the course of the weight gain from birth to five.

Summary

During the years 1925-32 the late Professor Alexander Low measured a series of 65 boys and 59 girls at birth and at subsequent birthdays up to and including age 5. Twenty-one physical measurements were taken and the raw measurements on each individual were published recently (Low, 1952).

We have traced, remeasured, and somatotyped as adults aged 25-30, 65% of those individuals, that is, 42 men and 38 women.

The means and standard deviations at each age, including adulthood, are given for measurements of supine body length, weight, head length and breadth, shoulder and hip breadths and length of lower arm and foot.

We have examined the constancy of growth pattern during the first five years and the relation of growth and physique at this time to adult physique. Part of our results are reported here, and part will appear in later papers. In this paper are given the matrix of correlation coefficients for ages 0, 1, 2, 3, 4, 5 and adult for each of the measurements mentioned, and also the percentage of adult variance of each measurement accounted for by multiple regression on the childhood measurements. Thus the percentage variance of adult body length accounted for by length at birth is 5%, by a combination of length at birth and 1 year 45%; by combination of 0, 1 and 2 years 59%; 0, 1, 2 and 3 years 64%; 0, 1, 2, 3 and 4 years 66%; and 0, 1, 2, 3, 4 and 5 years 66%.

The chief results are as follows:

(*a*) Correlations of all birth measurements with later measurements are much lower than the intercorrelations of later measurements between themselves. Thus for lower arm length all the birth correlations are in the range 0·10-0·35, whereas all 1-year and subsequent correlations are over 0·65. It is evident that the size of the newborn baby is only very slightly related to the size of the adult, or even to the size of the 2-year-old. The evidence of other studies agrees with this and supports the conclusion that prenatal environment during the last two months of pregnancy is the major determinant of newborn size, this prenatal environment depending to a considerable extent on the hereditary characteristics (such as uterine size) of the mother. The inherent growth characteristics of the child assert themselves after birth, however, and the correlations of childhood measurements with adult measurements rise sharply; for example, for supine length from 0·27 at birth to 0·67 at 1 year, 0·75 at 2 years and 0·79 at 3 years. The correlations for most measurements rise relatively little from 2 to 3 years and from 3 to 5 years not at all, on average. It seems that prediction of adult size can be made just as well from age 3 as from age 4 or 5. These results imply nothing as to the predictability of adult shape, a subject we are now examining.

The largest of the birth-adult correlations is for body weight, but this is only 0·40; the correlation with adult weight rises less than those of other measurements with increasing age and is 0·53 at age 5. The amount of male adult variance in weight accounted for by all the previous measurements from 0 to 5 is 42% compared with 67% for supine length.

(*b*) The cumulative multiple regression figures (percentage of adult variance accounted for at increasing ages) support these conclusions and add the information that the rate of growth from birth to 5 years has only a very small effect on adult measurements. Rate and size seem practically independent.

(*c*) Some sex differences in the measurements appear to be present and are described.

We must emphasize that these data, like those of all longitudinal studies, have their own peculiar characteristics, particularly in regard to subject selection and to environment during growth. Conclusions drawn from them may at least in detail be inapplicable to other samples. There is a great need for similar studies to be undertaken on other groups, to discover how far the generalizations given in this paper hold true for all growing children.

Much of this work was done while one of us (J.M.T.) was Ernest Hart Memorial Scholar of the British Medical Association. We wish to thank the B.M.A. for this support, without which this research would not have been possible.

Miss A. M. Clark, Professor Low's secretary, had a remarkable knowledge of the families concerned, and it is largely due to her enthusiasm that so many persons were traced after a lapse of nearly 25 years. We wish to record our grateful thanks for her staunch cooperation.

We wish also to thank Professor A. A. Moncrieff and Dr. F. Yates, F.R.S., for their critical encouragement; and, finally, to put on record our use of the Elliott Mark I electronic computer, without which we literally could not have made more than a fraction of the calculations these data call for.

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APPENDIX

List of Corrections Made in Aberdeen Records

Details of criteria for correcting are given in the text. Only head length, head breadth, height (or supine length), biacromial and bitrochanteric widths, foot length, cubit and body weight have been examined. The corrected measurement reads as follows:

Dimension	Sex	Case Number	Age	Corrected Measurement
Head length	M	6	1	171
Head breadth	M	6	1	135
Height	M	2	3	986
	M	4	1	767
	M	6	4	1,030
	M	7	2	906
	M	11	5	1,038
	M	13	4	1,020
	M	35	3	887
	M	38	5	980
	M	43	3	905
	M	54	1	755
	M	65	4	850
	F	6	3	990
	F	9	2	820
	F	10	2	830
Biacromial	M	2	5	250
	M	16	1	172
	M	32	1	170
	M	50	3	228
Bitrochanteric	M	4	1	146
	M	9	1	147
	M	24	5	181
	M	38	3	175
	M	50	1	145
	M	64	1	126
	F	4	1	150
	F	10	5	180
	F	23	5	188
	F	54	5	197
Foot length	M	42	4	147
	M	54	5	153
	F	53	3	136
Cubit	M	8	4	270
	M	56	1	185
	M	64	3	215
	F	3	2	225
	F	4	4	280
	F	6	1	194
	F	18	1	186
	F	23	4	256
	F	40	1	176

INFANT GROWTH

BY

JOHN THOMSON

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(RECEIVED FOR PUBLICATION APRIL 5, 1956)

Current literature on the growth of British infants is particularly concerned with studies of weight and weight gain, there being relatively little to be found concerning other measurements of body size and their rate of increase.

Because of this and because the mean size of the present day 6-month-old infant is greater than that of 30 years ago (Thomson, 1954), this investigation into infant growth has been made.

Source of Material

The infants concerned in this investigation were born in the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, and attended the Child Welfare Clinic in that hospital. An accurate record of the birth weight was available. Only healthy singleton legitimate infants were dealt with and in an attempt to eliminate the prematurely and postmaturely born the investigation was confined to infants whose birth weight was over 5½ lb. but not over 9½ lb. Since a few prematurely born infants weigh more than 5½ lb. and some postmaturely born infants weigh less than 9½ lb., selection on this basis may not absolutely confine the investigation to maturely born infants. The infants were drawn from Social Classes III, IV and V.

Method

In general, enquiries of this nature take one of two forms; they may be longitudinal or latitudinal, the latter being also referred to as cross-sectional. In the longitudinal method the same infant is observed at predetermined ages throughout the year. This method is difficult to carry out because the attendance of the infants at predetermined intervals is influenced by many factors, not the least of which are the weather and the degree of cooperation of the mother.

In the present enquiry the longitudinal approach was attempted but the wastage of observations being great, the method was abandoned and a latitudinal approach adopted. In this method all infants, whether attending the clinic regularly or not, were weighed and measured. From the accumulated data, observations made at ages of 2 weeks ± 2 days; 4, 8, 12, 16, 20 and 24 weeks all ± 3 days; 28, 32, and 36 weeks all ± 5 days; and 40, 44, 48 and 52 weeks all ± 7 days were abstracted, and used to construct Tables 1a, b and c, and 5a, b and c.

Clearly in this method an element of the longitudinal approach is incorporated since infants reappear irregularly at various age levels. Moreover, since weighing and measuring did not cease after the observations for the construction of Table 1a, b and c had been abstracted, it should be stated that Table 5a, b and c is not constructed from data contained solely in Table 1a, b and c.

As infants grow older attendances at clinics tend to become less frequent and may even cease before the infant is a year old. This represents a falling off in the availability of material and is in part compensated for by allowing a greater age range with increasing age of the infant.

A supervised pupil midwife weighed the naked infant to the last complete ounce on a beam balance using a sliding weight. The supine crown-heel and crown-rump lengths were measured by me. I used a specially constructed measuring board of my own design (Fig. 1). The board had a fixed curved perspex footpiece which allowed of hip and knee flexion when measuring crown-rump lengths, adequate side flanges to prevent distortion of the

FIG. 1.—Crown-heel and crown-rump measuring board (incorporates a writing board).

TABLE 1A
WEIGHT IN FIRST YEAR

Age (Wk.)	No.		Birth Weight				Actual Weight			
			Male		Female		Male		Female	
			Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
	M.	F.	(lb. oz.)	(oz.)	(lb. oz.)	((oz.)	(lb. oz.)	(oz.)	(lb. oz.)	(oz.)
2	209	201	7 6·56	14·7	7 3·77	15·3	7 8·41	13·80	7 5·07	15·03
4	190	196	7 6·37	15·5	7 3·19	14·8	8 7·51	18·25	8 2·87	15·23
8	228	211	7 6·73	14·9	7 3·92	13·7	10 7·96	21·59	10 0·61	17·12
12	194	188	7 7·36	14·1	7 3·35	14·0	12 8·08	23·40	11 10·50	20·83
16	196	159	7 5·68	14·8	7 3·36	14·1	13 14·88	25·42	13 3·55	21·22
20	170	155	7 6·05	14·5	7 3·79	14·3	15 6·38	25·75	14 7·25	24·18
24	163	153	7 6·59	14·4	7 2·91	15·1	16 12·19	28·38	15 10·81	28·30
28	159	159	7 6·10	13·1	7 3·51	14·6	17 15·27	30·95	16 13·36	29·27
32	165	161	7 4·94	13·9	7 4·17	14·3	18 14·95	30·61	17 14·30	32·32
36	173	153	7 6·25	14·2	7 3·44	13·6	19 14·94	29·01	18 10·58	32·46
40	157	151	7 5·45	14·5	7 4·48	14·6	20 8·52	30·22	19 6·81	32·77
44	142	142	7 5·14	14·2	7 5·79	14·5	21 6·58	34·04	20 5·74	36·35
48	153	133	7 5·04	13·2	7 5·83	13·9	22 2·22	38·28	20 14·63	37·62
52	131	130	7 4·79	13·1	7 6·72	15·3	22 12·37	38·13	21 11·20	37·65

TABLE 1B
CROWN-HEEL AND CROWN-RUMP LENGTH IN FIRST YEAR

Age (Wk.)	Crown-heel				Crown-rump			
	Male		Female		Male		Female	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)	(mm.)
2	517·30	20·23	509·55	19·90	347·13	14·56	342·39	13·44
4	533·00	18·85	525·46	19·52	359·59	13·33	353·46	13·72
8	565·79	20·98	557·03	19·20	381·43	15·82	374·84	11·65
12	596·61	19·64	582·55	18·92	401·31	15·12	389·56	14·70
16	619·81	16·02	604·13	17·94	414·62	15·30	404·19	13·34
20	639·52	20·36	623·12	14·67	427·31	15·26	414·26	12·39
24	657·91	19·83	641·42	19·77	437·26	12·69	423·53	14·83
28	673·69	19·40	656·80	20·47	444·94	15·68	432·49	14·07
32	688·25	19·77	673·14	22·20	453·23	14·63	441·51	15·67
36	704·43	16·94	686·59	21·60	461·17	14·33	447·80	16·27
40	714·91	21·45	699·35	20·93	467·82	15·51	453·97	16·05
44	728·77	22·35	712·75	23·29	473·71	15·79	462·03	18·41
48	739·44	23·27	725·31	23·99	479·85	16·38	467·59	18·86
52	750·53	22·70	738·80	25·64	484·61	16·12	475·94	20·50

TABLE 1C
OCCIPITO-FRONTAL CIRCUMFERENCE AND THORACIC CIRCUMFERENCE IN FIRST YEAR

Age (Wk.)	Occipital Frontal Circumference				Thoracic Circumference			
	Male		Female		Male		Female	
	Mean (mm.)	S.D. (mm.)	Mean (mm.)	S.D. (mm.)	Mean (mm.)	S.D. (mm.)	Mean (mm.)	S.D. (mm.)
2	361·70	11·61	354·12	12·12	333·51	17·83	327·47	16·54
4	373·11	11·75	364·30	11·40	347·81	17·00	345·69	15·34
8	390·34	11·43	381·67	10·67	374·55	18·00	370·25	14·80
12	403·92	11·30	394·51	11·23	396·66	18·06	387·37	17·53
16	414·85	11·40	406·01	10·88	410·04	18·26	402·48	17·35
20	426·49	11·04	417·13	10·56	416·50	19·72	412·75	18·56
24	436·71	11·61	424·81	10·53	433·22	18·79	425·52	18·74
28	444·45	11·79	433·25	11·07	442·99	19·81	434·05	20·69
32	451·41	12·14	440·47	12·60	451·00	18·67	442·78	21·07
36	458·20	11·55	445·49	11·66	459·09	18·86	448·62	21·43
40	462·27	11·90	450·70	11·61	464·06	18·98	454·52	18·75
44	466·84	11·01	454·96	12·92	469·73	19·02	461·65	21·50
48	470·57	11·98	457·95	12·32	473·67	20·47	465·26	22·35
52	473·83	11·72	462·12	11·92	481·62	18·97	470·87	21·69

Conversion Factors. 1 mm.=0·039370113 in. 1 oz.=28·34953 gr. 1 lb.=453·5924 g.

sliding headpiece and a writing ledge on which to note observations. A steel millimetre scale was incorporated in the base of the board. Lengths were read to the last complete millimetre. The occipito-frontal circumference was measured by placing an accurately graduated millimetre linen tape closely round the head and over the most prominent parts of the frontal and occipital bones. The circumference of the thorax was measured at nipple level with the infant lying on the back on a firm flat mattress. The reading was made at what was considered to be midway between inspiration and expiration. The same tape was used for both circumferential measurements, and was read to the last complete millimetre. The tape was checked frequently against the steel millimetre scale on the measuring board and replaced when an error was shown. I had the assistance of the Sister in charge of the Clinic when I made these measurements and I was unaware of previously recorded measurements.

Results

From the data obtained, the means of weight, crown-heel length, crown-rump length, occipito-frontal circumference and thoracic circumference with their respective standard deviations have been calculated for each sex at each age point (Tables 1a, b, c).

However, because McKeown and Gibson (1951) showed that the mean birth weight of firstborn infants was less than the mean birth weight of subsequently born infants, these tables have been compiled from observations made on infants born of first pregnancies. More than 100 observations were included in each sex age group for each measurement. All computations were made by me.

Discussion

Mean Values. Considering that the present enquiry was confined to infants born of first pregnancies and who were within a restricted birth weight range and social grouping, the mean values of weight now reported compare favourably with those of Parfit (1951) for Oxford infants. In addition the 52 week mean value is similar to that given by Hewitt and Stewart (1952) for firstborn Oxford infants. The values for weight and length compare favourably with the data of Norval, Kennedy and Berkson (1951) for Rochester, Minnesota, infants, but when comparison is made with the Brush Foundation data (Simmons, 1944), the Edinburgh mean weights, crown-heel and crown-rump lengths are lower. In making this latter comparison it is noted that the higher means of the Brush Foundation are 'derived from the measurements of a selected sampling of 999 white children, the majority of whose parents are above average both in education and in economic level and who are of North European ancestry'. The occipito-frontal circumference means are similar to those reported by Vickers and Stuart (1943) for Boston, U.S.A., infants, and while in the first six months of life they resemble the data of Meredith (1946) for Iowa infants in the second six months they exceed Meredith's data. By contrast the present data are lower than the means published by Bayley and Davis (1935) for Berkeley, California, infants.

It is important to compare the present data not only with contemporary data but also with publications of earlier years, especially when these earlier publications deal with infants in the same country and in the same part of the country. Comparison can be made with Paton and Findlay (1926) who give means for weight, crown-heel and crown-rump lengths for Edinburgh infants. In this connexion, weight has already been considered (Thomson, 1955) and shown to be greater than that reported by Paton and Findlay. The present publication shows that the mean crown-heel and crown-rump lengths are also greater than those reported by Paton and Findlay (Table 2). The means for weight, crown-heel and crown-rump lengths, occipito-frontal and thoracic circumferemces reported in Low's tables (1952) for Aberdeen infants born in the years 1923-27 are all less than the mean figures now published. Such observations suggest that, as has already been shown in the case of weight (Thomson, 1955), the length norms in use in welfare clinics may require alteration. Workers in welfare clinics are commonly provided with crown-heel norms only, and these, generally undifferentiated for sex, are presented as a graph. The present data have been recalculated on this basis and compared with the graphs which have been in use by three local authorities for many years. Two of the local

TABLE 2

CROWN-HEEL AND CROWN-RUMP LENGTH (PATON AND FINDLAY, 1926)

Age (month)	Crown-heel (mm.)		Crown-rump (mm.)	
	Male	Female	Male	Female
1	524·88	522·82	340·61	342·39
3	581·16	565·25	373·13	362·46
6	628·80	621·44	399·80	395·22
9	675·07	655·86	420·88	412·75
12	699·82	698·82	439·42	435·86

authorities have used the same graph (Fig. 2). It is clear that the crown-heel norm now published for Edinburgh infants is, throughout the year, consistently greater than that which was prepared by the late Dr. T. Y. Finlay, Maternity and Child Welfare Officer for Edinburgh, when he collaborated some 30 years ago with Paton and Findlay, and which is still in use in Edinburgh clinics. The origin of the graph used by the other two authorities is not disclosed. It appears to be the same as the graph which was used in the investigation planned and carried out by Paton and Findlay, since a copy of it appears in the appendix to their report. The graph is not the result of Paton and Findlay's investigations. The first six months covered by this graph are approximately the same as the findings of the present investigation. Thereafter, the form of the graph is completely at variance with the present investigation as well as with the graph for Edinburgh infants by Finlay.

From these observations one may conclude that the mean crown-heel length of infants today is greater than formerly and that the norms of crown-heel length as well as of weight in general use by child welfare clinics are in need of revision.

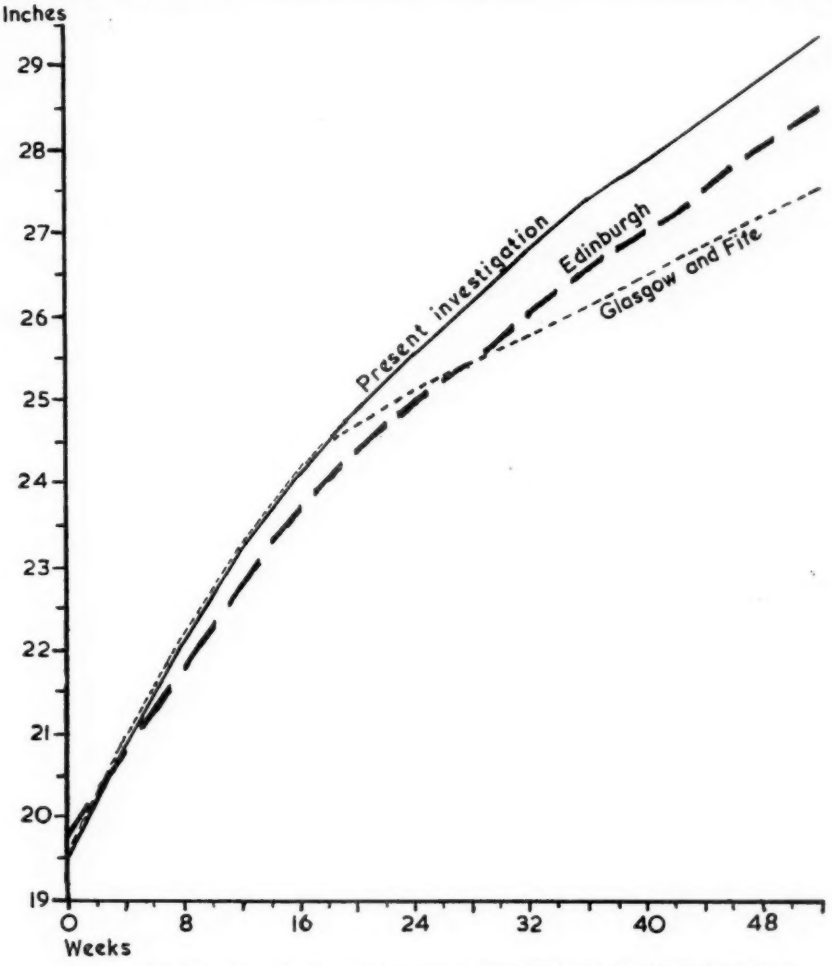

FIG. 2.—Crown-heel length derived from present investigation and welfare clinic norms.

The Influence of Sex. In each of the measurements, boys' are consistently greater than girls' (Tables 1a, b, c), and the amount of the difference is more at the end of the year than at the beginning. Nevertheless, if the male excess is expressed as a percentage of the female mean (Table 3, Fig. 3) only in the case of weight is the year-end difference much greater than that at the beginning of the year. This relatively greater increase in male weight is concentrated into the first 12 weeks of the year, after which there is a period of relatively level growth by the sexes followed by a decline in the percentage difference in the last 12 weeks of the year.

The crown-heel and crown-rump differences show a similar pattern. In the case of the occipito-frontal circumference the pattern is rather that of a slight

TABLE 3
PERCENTAGE BY WHICH A MALE MEAN MEASUREMENT EXCEEDS FEMALE MEAN MEASUREMENT

Age (wk.)	Weight	Length		Occipito-frontal Circumference
		Crown-heel	Crown-rump	
2	2·8	1·5	1·4	2·1
4	3·5	1·4	1·7	2·4
8	4·6	1·6	1·8	2·3
12	7·3	2·4	3·0	2·4
16	5·4	2·6	2·6	2·2
20	6·5	2·6	3·1	2·2
24	6·9	2·6	3·2	2·8
28	6·6	2·6	2·9	2·6
32	5·8	2·2	2·7	2·5
36	6·8	2·6	3·0	2·9
40	5·7	2·2	3·1	2·6
44	5·2	2·2	2·5	2·6
48	5·9	1·9	2·6	2·8
52	4·9	1·6	1·8	2·5

but definite relatively greater male increment spread unevenly over the year. The thoracic difference

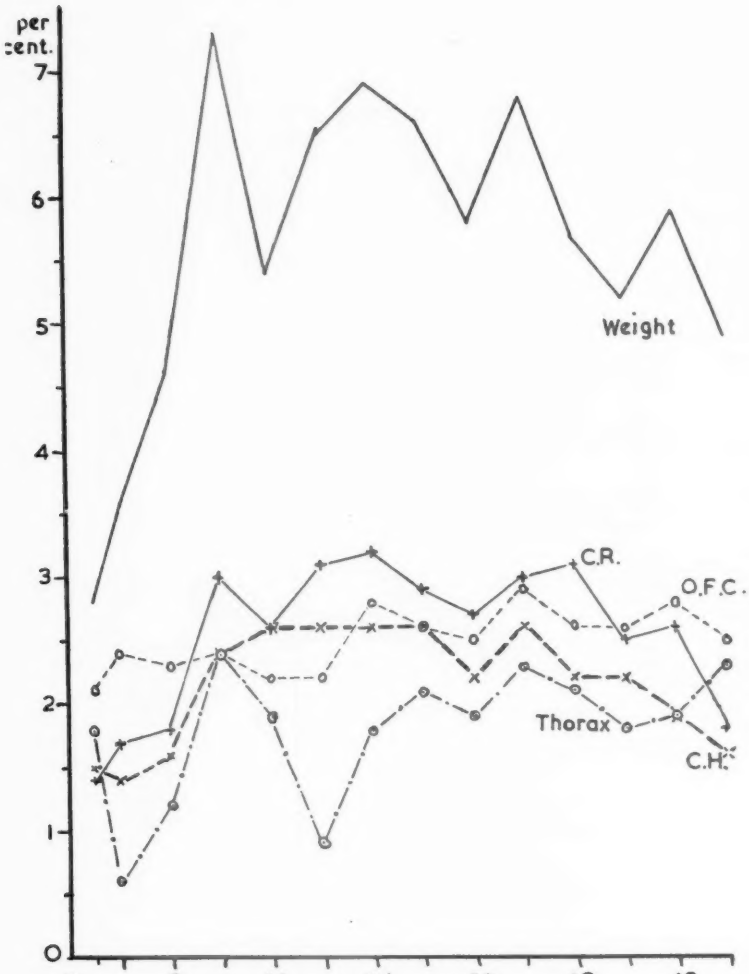

FIG. 3.—The percentage by which ▪ male mean measurement exceeds ▪ female mean.

fluctuates more in the first 24 weeks than any other measurement and in the remainder of the year shows a small but relatively greater male increment.

In considering the graphs (Fig. 3) it is well to remember that they are a representation of the difference between two means, that means are estimations, and are liable to some variation.

A similar trend in the sex difference concerning weight and length, though perhaps less marked in the case of weight, is shown by the data of Norval *et al.* (1951) while a decline in the percentage at the end of the year can be demonstrated in the weight, crown-heel and crown-rump lengths of the Brush Foundation data (Simmons, 1944) which unfortunately do not contain measurements at or near to birth.

For the same crown-heel length Norval *et al.* (1951) state that male infants are heavier than female. One cannot prove this by comparing groups of male and female infants who are of the same mean length and mean age. After the age of 8 weeks, owing to the greater length increment of male infants, sizable matched groups cannot be obtained. One may compare male and female groups of the same mean length provided the age distribution of the groups is symmetrical. On this basis one cannot proceed with the present data beyond a mean length of 695·5 mm. drawn from the range 690-699 mm. At this length the mean age for 122 female infants is 39 weeks ranging from 24 to 52 weeks and the mean weight is 305·93 oz. The corresponding figures for 115 male infants are 35½ weeks ranging from 20 to 48 weeks and 308·8 oz.; not an impressive difference in weight. It is to be noted that the findings of Norval *et al.* (1951) are based on observations carried well into the second year of life.

It has been shown (Thomson, 1955) that in both sexes one-quarter, one-half and three-quarters of the mean weight gain for the year is achieved at approximately the same age. The approximate ages at which these fractions of the other mean increments are achieved are given in Table 4. The crown-heel growth and occipito-frontal growth appear to

TABLE 4
APPROXIMATE AGE IN WEEKS AT WHICH ONE-QUARTER, ONE-HALF AND THREE-QUARTERS OF MEAN GAIN FOR THE YEAR IS ACHIEVED

		Fraction of Year Gain		
		¼	½	¾
Weight		10	19-20	32
Crown-heel		10	19-20	34
Crown-rump	Male	8	16	32
	Female		18	
Occipito-frontal circumference		8	16	28
Thorax	Male	7	18	33
	Female		17	28

proceed at the same relative rate in each sex; but, while crown-heel growth rate resembles the weight growth rate, the occipito-frontal growth is faster. In the crown-rump growth rate there may be a slight sex difference at 16 to 18 weeks but it is not sustained. A sex influence may exist in the thoracic growth because the female appears to gain size more rapidly, three-quarters of the year's gain being made four weeks before the male. In considering these rates of growth it should be remembered that, unlike weight which is calculated from birth, the lineal measurements are calculated from 2 weeks of age.

Variability. The standard deviations of the various measurements do not display a sex bias. Weight shows a steady increase in the standard deviation throughout the year and conforms to the findings of all other investigators.

The thoracic measurements and the two length measurements show a wider standard deviation at 52 weeks than at 2 weeks. This is also shown for length by Boyd (1948) and for length and circumference of thorax by Low's tables. The Brush Foundation data also display an increase in the standard deviation with an increase in age. Norval *et al.* (1951) reported no decided change in the standard deviation for length in either sex throughout the year.

The present investigation shows no increase in the standard deviation of the occipito-frontal circumference. This is similar to Meredith (1946), Vickers and Stuart (1943), Bayley and Davis (1935) and Boyd (1948). It is noted, however, that particularly in the female infant Low's tables show a greater standard deviation at 52 weeks than at 3 days.

Increment. A table of weight increment covering the first year has been published and discussed (Thomson, 1955). It was shown that while the standard deviation of weight increment increased with age the coefficient of variation declined. This pattern is also present in the increment tables for crown-heel and crown-rump length and for occipito-frontal circumference measurements (Tables 5a, b, c).

It is well known that post-natal measurements whether of weight or length correlate positively and significantly with the same measurement made at or near to birth. Further, a group of infants who at birth have a mean weight of 1 lb. greater than the mean weight of another group, will at a year old have a mean weight approximately 1 lb. greater. Because of these observations there is a tendency to assume that a measurement made at or near to birth determines the subsequent measurement in the individual child and by implication determines the post-natal increment.

In the case of weight, this aspect of growth has already been investigated (Thomson, 1955). It has been shown 'that the correlation coefficients between birth weight and post-natal weight gain were not of statistical significance, and were almost uniformly negative'. It was also suggested 'that there is a strong tendency for infants of lesser birth weight to gain weight more rapidly than infants of greater birth weight'.

Because of these findings concerning weight increment, it was thought desirable to examine the relationship between crown-heel and crown-rump lengths and the occipito-frontal circumference at 2 weeks and at subsequent ages throughout the first year. The correlation coefficients obtained for the two sexes are given in Table 5a, b, c.

In all three measurements the correlation coefficients are negative and statistically significant. This suggests a strong tendency for infants who are short at 2 weeks old or who have small heads at 2 weeks to gain size more rapidly than those who are longer or who have larger heads.

This finding is in large measure confirmed by Low's tables which also yield, for the same dimensions, negative correlation coefficients when the first year increment is related to the 3-day measurement, the sexes again being examined separately. However, in the case of the male crown-heel length in Low's tables this negative correlation coefficient is not statistically significant.

Absence of significance in this particular group is of little moment since it appears to be due to the presence of at least two infants who deviate far from normal standards. One of these infants measured 25 in. at a year old and the other 26 in., while their respective weights at a year old were 14·10 lb. and 15·75 lb. In this connexion it should be pointed out that the foreword to Low's tables does not say whether all the measurements were derived from normal healthy children. The inclusion in the tables of a girl whose weight is a quarter-pound less at 4 years than it was at 3 years serves to emphasize this doubt.

Although the correlation coefficients presented are statistically significant the degree of association is not a high one. It is about 40% of a complete correlation, with the crown-rump measurement showing a rather closer relationship than the other two measurements. The consistent presence of the negative sign may be of more importance than the presence of significance since there are other factors than size at or near to birth which may be related to subsequent increment and which play a part in

TABLE 5A

CROWN-HEEL INCREMENT CORRELATED WITH CROWN-HEEL LENGTH AT 2 WEEKS ±2 DAYS

Age (Wk.)	Number		Crown-heel Length at 2 Weeks (mm.)				Crown-heel Increments (mm.)						Correlation Coefficient		Standard Error	
			Male		Female		Male			Female						
	M.	F.	Mean	S.D.	Mean	S.D.	Mean	S.D.	C.V.	Mean	S.D.	C.V.	Male	Female	Male	Female
4	137	118	518·9	18·4	508·5	21·1	16·6	6·9	41·6	17·8	8·3	46·6	−0·20	−0·36	0·086	0·092
8	114	99	516·1	20·0	509·4	20·6	49·4	11·0	22·3	47·6	11·5	24·2	−0·18	−0·27	0·094	0·101
12	135	116	517·8	19·9	509·2	21·1	79·6	10·5	13·2	74·0	12·1	16·4	−0·25	−0·37	0·086	0·093
16	128	105	517·3	20·3	509·8	19·6	101·9	12·5	12·3	96·1	13·4	13·9	−0·44	−0·37	0·089	0·098
20	120	97	519·4	19·0	509·9	21·0	120·2	13·3	11·1	115·4	13·6	11·8	−0·41	−0·45	0·092	0·102
24	125	96	521·0	18·9	509·1	21·9	137·8	14·4	10·4	132·9	14·7	11·1	−0·33	−0·45	0·090	0·103
28	124	106	519·4	18·7	509·5	21·7	155·6	16·2	10·4	148·5	16·1	10·8	−0·40	−0·48	0·090	0·098
32	117	96	519·0	18·8	510·6	20·6	170·3	17·1	10·0	164·7	17·8	10·8	−0·45	−0·37	0·093	0·103
36	117	90	518·7	19·1	510·3	19·9	183·9	17·1	9·3	177·6	18·2	10·2	−0·47	−0·39	0·093	0·106
40	94	96	518·9	20·4	509·6	20·4	196·7	18·1	9·2	190·5	19·0	10·0	−0·39	−0·41	0·104	0·103
44	80	99	516·5	21·8	511·7	19·0	209·9	20·0	9·5	201·1	19·4	9·6	−0·40	−0·29	0·101	0·101
48	98	80	517·3	20·4	509·9	20·2	221·8	19·5	8·8	214·0	21·8	10·2	−0·36	−0·31	0·102	0·113
52	100	88	516·1	20·7	512·2	19·0	233·0	20·1	8·6	225·4	20·2	9·0	−0·39	−0·29	0·100	0·107

TABLE 5B

CROWN-RUMP INCREMENT CORRELATED WITH CROWN-RUMP LENGTH AT 2 WEEKS ± 2 DAYS

Age (Wk.)	Crown-rump Length at 2 Weeks (mm.)				Crown-rump Increment (mm.)						Correlation Coefficient	
	Male		Female		Male			Female				
	Mean	S.D.	Mean	S.D.	Mean	S.D.	C.V.	Mean	S.D.	C.V.	Male	Female
4	348·0	14·0	341·2	15·0	12·4	8·2	66·1	11·6	6·7	57·8	−0·35	−0·26
8	345·2	14·8	341·2	14·7	35·2	9·9	28·1	33·9	9·8	28·9	−0·27	−0·37
12	347·4	14·8	341·1	14·9	53·8	11·5	21·4	49·7	10·6	21·3	−0·34	−0·47
16	347·3	15·3	340·0	14·6	67·5	12·3	18·2	63·6	12·8	20·1	−0·47	−0·51
20	348·6	14·5	341·6	15·6	78·4	14·9	19·0	74·6	12·1	16·2	−0·41	−0·57
24	349·0	14·9	342·2	15·8	88·2	14·6	16·6	82·8	12·7	15·3	−0·46	−0·57
28	348·1	14·5	341·8	15·5	98·2	15·3	15·6	92·3	14·3	15·5	−0·54	−0·59
32	348·0	14·5	342·2	14·8	105·8	16·4	15·5	100·3	15·1	15·1	−0·48	−0·50
36	348·0	15·0	341·3	15·4	113·3	16·4	14·5	105·5	15·5	14·7	−0·56	−0·60
40	347·7	14·6	341·6	15·5	120·0	15·7	13·1	110·6	15·1	14·0	−0·58	−0·63
44	347·0	14·9	343·3	15·2	125·5	16·7	13·3	116·9	17·1	14·6	−0·50	−0·54
48	347·5	14·5	341·2	15·3	132·0	16·5	12·5	124·7	19·4	15·5	−0·50	−0·39
52	346·1	15·8	343·4	15·8	137·5	17·9	13·0	130·3	18·9	14·5	−0·56	−0·47

TABLE 5C

OCCIPITO-FRONTAL CIRCUMFERENCE INCREMENT CORRELATED WITH OCCIPITO-FRONTAL CIRCUMFERENCE AT 2 WEEKS ± 2 DAYS

Age (Wk.)	Occipito-frontal Circumference at 2 Weeks ± 2 Days				Occipito-frontal Circumference Increment						Coefficient Correlation	
	Male		Female		Male			Female				
	Mean	S.D.	Mean	S.D.	Mean	S.D.	C.V.	Mean	S.D.	C.V.	Male	Female
4	362·1	11·4	353·0	11·7	11·9	5·6	46·7	10·5	4·5	42·4	−0·25	−0·25
8	360·9	12·4	353·2	11·9	28·2	7·2	25·3	28·3	7·0	24·6	−0·37	−0·42
12	361·0	12·3	353·0	11·8	43·4	8·0	18·5	41·4	7·4	17·8	−0·32	−0·41
16	360·4	12·4	353·8	11·2	54·4	8·9	16·3	52·7	8·4	15·9	−0·36	−0·47
20	361·8	12·2	354·1	11·5	64·8	9·2	14·1	62·8	8·5	13·5	−0·43	−0·50
24	362·5	12·4	354·0	11·6	74·3	10·1	13·6	71·4	9·3	12·9	−0·44	−0·51
28	362·5	12·4	353·7	11·4	82·7	10·2	12·4	79·1	9·9	12·5	−0·49	−0·45
32	361·3	12·6	354·4	11·5	90·1	11·3	12·5	85·3	10·9	12·8	−0·42	−0·45
36	361·8	12·3	353·6	11·3	95·5	11·5	12·1	92·2	10·7	11·6	−0·44	−0·46
40	361·4	12·5	354·2	11·1	101·1	11·3	11·2	96·8	11·4	11·8	−0·52	−0·49
44	361·9	12·6	355·2	11·3	105·4	11·9	11·3	100·3	11·9	11·9	−0·63	−0·49
48	361·1	11·5	353·8	11·5	109·4	12·3	11·2	104·8	13·3	12·6	−0·39	−0·40
52	359·9	12·8	355·0	11·3	112·4	12·9	11·5	107·6	13·2	12·3	−0·47	−0·57

determining the pattern of infant growth. The present findings should not be interpreted to mean that of any two individual infants the one who is smaller at birth will certainly grow faster than the other: the tendency is that way, it is not a certainty.

Summary

Based on 2,430 sets of observations of males and 2,292 sets of observations on females, means with standard deviations for weight, crown-heel and crown-rump lengths, occipito-frontal and thoracic circumferemces of Edinburgh infants are presented. They cover the first year of life at four-week intervals. The observations were made on legitimate, singleton, first pregnancy infants whose birth weights were within the range of over 5½ to 9½ lb.

Mean measurements now reported are greater than those of Paton and Findlay or of Low, while the mean crown-heel length undifferentiated for sex is appreciably greater than that in use in Edinburgh welfare clinics.

There is a significant negative correlation coefficient between measurements at 2 weeks and the subsequent increment. This suggests a strong tendency for infants who are small at birth to grow more rapidly than infants who are bigger.

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PREMATURITY IN EDINBURGH

BY

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During the period 1952 to 1954 a group of babies born prematurely to mothers delivered in two Edinburgh maternity hospitals, together with a group of full-time infants, were enrolled in a long-term developmental survey. In order to provide some comparative information about all babies born during that period certain data were obtained about all births in Edinburgh during the 12 months October, 1953, to October, 1954. This information was considered of sufficient interest to be presented in a separate paper.

All births in Edinburgh are notified to the Public Health Department of the Corporation as being under or over 5½ lb. at birth. Access to these records was allowed. Every premature birth together with one in 10 of all mature births was recorded. To reconstruct the total births in the subsequent analysis the figures for mature births have been multiplied by 10.

The following information was recorded about each birth: (1) birth weight, (2) legitimacy, (3) age of the mother, (4) parity, (5) occupation of the father in legitimate births, (6) date of marriage.

Birth weight, age of mother and parity were given in hospital records. When the baby was born at home this information was obtained by the Health Visitor at her first post-natal visit. In those cases in which the baby died or a stillbirth resulted in domiciliary confinements, the general practitioner or midwife attending the birth was asked to supply the information. During the period under review about 75% of births in Edinburgh took place in hospital and the recorded birth weights are likely to be accurate. In the case of domiciliary confinements, weights were usually recorded on a spring balance and will therefore be less accurate. The occupation of the husband and the date of marriage was obtained from birth certificate records by permission of the Registrar General for Scotland. The husband's occupation was classified according to the Registrar General's Index of Occupations, 1950, into five social classes (General Register Office, 1951). All the information was completed in about 95% of the total births.

* This work was done during the tenure of a grant from the Advisory Council for Medical Research of the Department of Health for Scotland.

Distribution of Birth Weight

During the period under review there were 7,157 births registered to mothers usually domiciled in Edinburgh. Births to mothers whose homes were outside the city boundaries were excluded.

A premature infant is taken to be one with a birth weight of 5½ lb. or less irrespective of the length of gestation, which was not recorded in many cases.

Table 1 gives the figures for premature and mature births, neonatal deaths and stillbirths in each group. Table 2 gives the birth weight distribution for

TABLE 1
TOTAL BIRTHS IN EDINBURGH, OCTOBER, 1953, TO OCTOBER, 1954

	Premature	Mature	All Births
Number	471	6,686	7,157
Neonatal deaths	63	48	111
Stillbirths	80	88	168
Percentage total births	6·58%	93·42%	100%
Neonatal deaths per 1,000	134	7·2	15·5
Stillbirths per 1,000	170	13·2	23·5

TABLE 2
BIRTH WEIGHT DISTRIBUTION OF LEGITIMATE AND ILLEGITIMATE BIRTHS

Birth Weight (lb. oz.)	Legitimate			Illegitimate		
	No.	% of Known Birth Weight	Cumulative %	No.	% of Known Birth Weight	Cumulative %
Premature(birth weight not known)	2					
2·8 and under	39	0·55	0·55	3	0·66	0·66
2·9–3·8	58	0·86	1·41	5	1·11	1·77
3·9–4·8	83	1·36	2·77	7	1·56	3·33
4·9–5·8	242	3·62	6·39	24	5·34	8·67
5·9–6·8	1,065	15·92	22·41	91	20·22	28·89
6·9–7·8	2,124	31·74	54·15	136	30·22	59·11
7·9–8·8	1,934	28·91	83·06	122	26·12	85·23
8·9–9·8	879	13·14	96·10	40	8·88	94·11
9·9 and over	258	3·90	100·00	22	4·89	100·00
Mature (birth weight not known)	13			2		
Total	6,697			452		

legitimate and illegitimate births. It will be seen that the percentage of premature births in the illegitimate group is 8·7 compared with 6·4 of legitimate births. This difference is statistically significant.

The Effect of Age on Birth Weight

Fig. 1 shows the proportion of babies 5½ lb. or less at birth, those weighing 5 lb. 9 oz. to 7 lb. 8 oz. and those over 7½ lb. in five age groups.

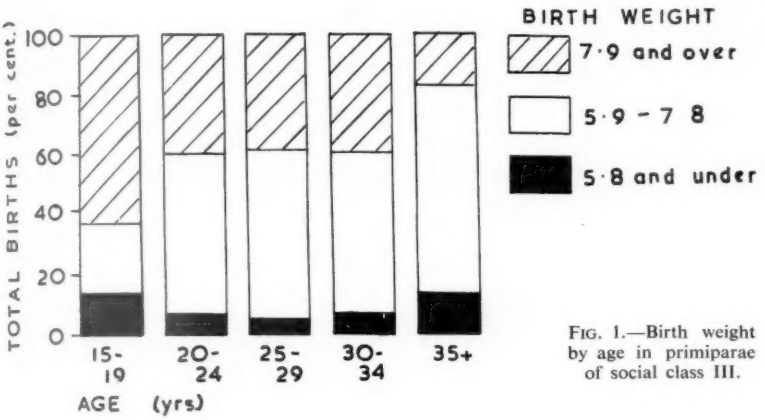

FIG. 1.—Birth weight by age in primiparae of social class III.

In subsequent sections it is shown that both parity and social class have an effect on birth weight, so in considering the effect of age only primiparae of social class III have been included.

It will be seen that the birth weight distribution is similar over the age period 20 to 34 years but in those under 20 years and over 35 years the prematurity rate is about twice as high. This increase is statistically significant.

A more striking difference is shown in the proportion of big babies, i.e., those over 7½ lb. at birth. More than 60% of all babies born to girls under 20 years were over 7½ lb. compared with 40% in the age group 20 to 34, and less than 18% in mothers of 35 years and over, at the time of their first birth.

The greater number of premature births in the youngest age group may be associated with the high incidence of premarital conception. Fig. 2 gives the frequency of premarital conception according to the age of mother for all births in Scotland in 1953 (Annual Report of the Registrar General for Scotland, 1953). It will be seen that 60% of all births to mothers under 20 years of age occurred less than eight months after marriage and 33% occurred less than six months after marriage.

In this analysis the baby was considered to have been conceived before marriage when the date of birth was less than 32 weeks after marriage in the case of full-time infants, and less than 24 weeks in the case of premature infants. On this basis in social class III, 36% of all babies were conceived before marriage in girls under 20 years, 15% in those between 20 and 24 years and 4% in those of 25 and over.

The birth weight distribution in the under-20 age group for premarital conceptions and others is shown in Table 3. The percentage of premature births in those infants conceived before marriage is 13·0 compared with 11·3 in the rest. The numbers are small and the difference is not statistically significant. However, the difference in the proportion of big babies, 43·5% in the premarital conception group and 76·3% in the rest, is highly significant.

Premarital conception increases steadily from social class I to social class V and it therefore seems probable that within social class III, which includes a wide variety of occupations, those who conceive before marriage tend to come from a poorer economic background. This would seem to be the explanation of the different birth weight dis-

TABLE 3
BIRTH WEIGHT DISTRIBUTION IN THE AGE GROUP 15 TO 19 YEARS IN SOCIAL CLASS III

Birth Weight (lb. oz.)	Premarital Conceptions (%)	All Births excluding Premarital Conceptions (%)
5·8 and under ..	13·0	11·3
5·9–7·8 ..	43·5	12·4
7·9 and over ..	43·5	76·3

FIG. 2.—Premarital conception by age of mother in Scotland, 1953.

tribution between those who conceive before and after marriage. It is striking that after the exclusion of premarital conceptions over three-quarters of all babies born to these young mothers were over 7½ lb. at birth.

A possible explanation of the higher prematurity rate amongst young mothers combined with a high proportion of big babies is that in some cases premature labour may be induced by efforts to get rid of an unwanted pregnancy.

It appears that from the biological point of view the youngest mothers are most successful in their pregnancies, though this does not mean that these babies do better subsequently. In the developmental study now in progress it has been found that the youngest mothers in general are less efficient in the handling of their babies, and for that reason later pregnancy is probably to be preferred.

The Effect of Social Class on Birth Weight

Fig. 3 shows the birth weight distribution in primiparae between the ages of 20 and 34 years in three social groups.

It will be seen that the prematurity rate in social classes I and II is less than one-half that in social classes IV and V; this difference is significant. The numbers of premature births in social classes I and II are so small that they have been amalgamated, but the percentage of large babies can be analysed in five social groups and is even more striking, as shown in Table 4. The proportion of large babies is more than twice as high in social class I as in social class V, after the effect of age and parity has been allowed for. This difference is highly significant.

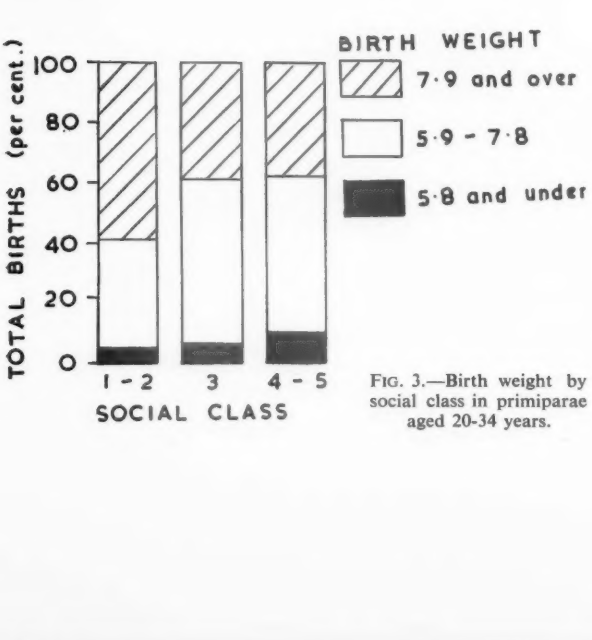

FIG. 3.—Birth weight by social class in primiparae aged 20-34 years.

The Effect of Parity on Birth Weight

Fig. 4 shows the percentage of premature births according to the parity of the mother for all births and separately for social classes I and II, and social classes III, IV and V. It is seen that for all births the highest prematurity rate is found with first births and the lowest with second births; subsequently the incidence of prematurity rises. However, when comparing mothers of social classes I and II with those in social classes III, IV and V, it is seen that the more prosperous mothers maintain their low prematurity rate with all births after the first. High birth ranks are infrequently encountered in this social group and the figures cannot be further analysed after the fourth birth, but in social classes III, IV and V the prematurity rate for sixth and subsequent births rises to nearly 18%. The obvious conclusion is that in the poorer homes every

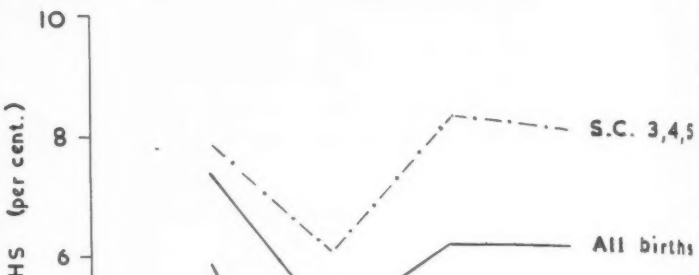

FIG. 4.—Prematurity by parity and social class.

TABLE 4
PROPORTION OF LARGE BABIES ACCORDING TO SOCIAL CLASS

Social Class	Total Births	Percentage of Babies over 7½ lb. at Birth
1	217	74·2
2	381	50·7
3	1,233	39·4
4	124	40·3
5	196	36·2

additional baby brings added financial strain and extra work and worry to the mother. An additional factor in the increase of prematurity with parity in this group is the short time between pregnancies in many cases. In middle class homes planned pregnancies are much more common and extra domestic help is usually available to the mother as her family increases.

A similar picture is seen when the national figures for stillbirth rates are analysed. Fig. 5 is based on the figures for stillbirths according to parity and social class given in the Annual Report of the Registrar General for Scotland, 1953. Here again in social class V the incidence of stillbirth rises

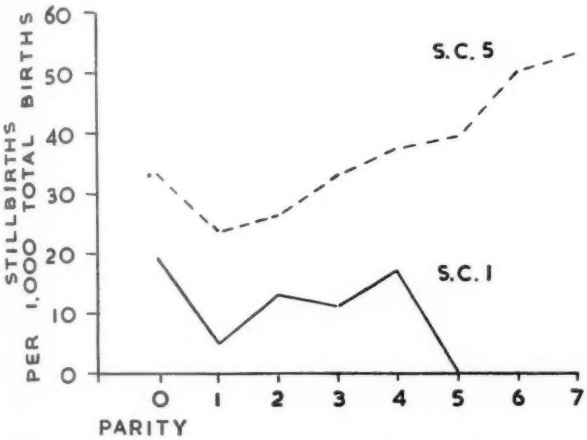

FIG. 5.—Stillbirth rates by social class and parity in Scotland, 1953.

steadily after the second birth whereas in social class I, although there is also a rise, the rate never reaches that of the first birth. The figure of 17 per 1,000 for fifth births is based on one case, and no stillbirths were recorded in subsequent parities in social class I.

Social Class Differences in Age of Mother at the First Birth

Fig. 6 shows the proportion of first births occurring in five age groups in three social classes. In social classes III, IV and V about half of the first births occur during the period 20 to 24 years though a substantial number, especially in social class V, occur before the age of 20. There were no births to primiparae under 20 years in social classes I and II. Here about half of the births occur in the age period 25 to 29 years.

The Interval Between Marriage and the First Birth

Fig. 7 shows the incidence of prematurity according to the interval between marriage and the first

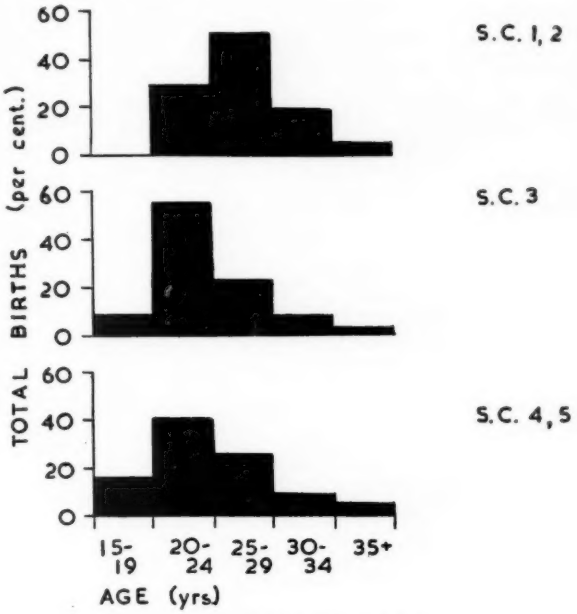

FIG. 6.—Age at first birth by social class.

birth in social classes I and II, and social classes III, IV and V in women aged between 20 and 34 years. It will be seen that a high incidence of prematurity (13·3%) occurred in cases of premarital conception in social classes III, IV and V. There were no recorded premarital conceptions in social classes I and II in the premature group. The incidence of prematurity is also significantly higher in all social classes in the case of birth occurring in the first year of marriage and also in those cases where the first birth was delayed until more than three years after marriage. In primiparae over the age of 34 years there is a high proportion of premature

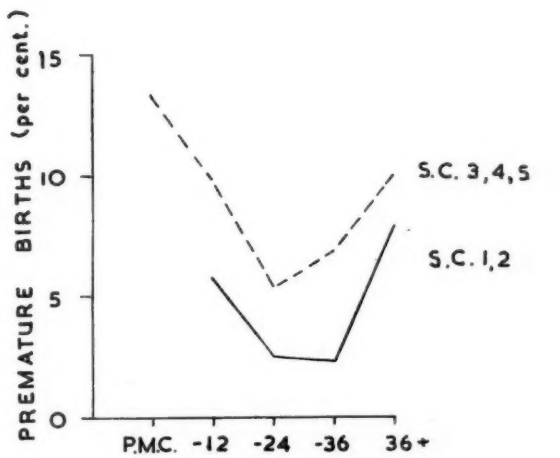

FIG. 7.—Incidence of prematurity in primiparae by time married.

births to mothers who have been married longer than three years, but these have been excluded to remove the effect on birth weight which may be due to age alone. It would be interesting to know the incidence of previous abortions, as it seems probable that subfertile mothers and those with an increased liability to miscarriage are also more likely to produce a premature infant.

Martin (1954), working on the figures for prematurity collected in the national enquiry into maternity in Great Britain carried out in 1946, also found a definite correlation between delay in conception and prematurity, although the frequency of prior miscarriage did not appear to differ significantly in the mature and premature groups.

A possible explanation of the higher prematurity rate in those who conceive shortly after marriage is that those from a more prosperous background may deliberately delay conception until they have settled into a home of their own.

One-third of all mothers in social classes III, IV and V conceived either before or shortly after marriage compared with one-quarter in social classes I and II, although the same proportion in all social classes (nearly 70%) had their first baby before the fourth year of marriage.

Summary

A statistical analysis of all births in Edinburgh, over a 12-month period, indicates the following:

(1) A significant increase of prematurity is found in illegitimate births.

(2) Under 20 years of age and over 34 years, the prematurity rate is twice that for the age period 20 to 34 years. The youngest mothers have a high proportion of big babies especially after excluding cases of premarital conception when three-quarters of the babies were over 7½ lb. at birth compared with one-fifth in mothers over 34 years.

(3) There is a significantly lower prematurity rate, and higher proportion of big babies born to mothers from a more prosperous economic background.

(4) The prematurity rate rises steadily after the second birth in the lower social classes. Mothers from social classes I and II maintain their low prematurity rate with all births after the first. Similar findings were observed for stillbirth rates using national figures.

(5) A high prematurity rate was found in babies conceived before marriage or shortly afterwards. The prematurity rate rises again with births delayed for more than three years after marriage.

It is a pleasure to thank Dr. H. E. Seiler and Dr. H. P. Tait, of the Public Health Department, Edinburgh Corporation, for allowing access to City records; Miss G. Pike, Superintendent of Health Visitors, for assistance in the collection of the data; Mr. A. D. Michie for permission to view birth certificate records; Dr. Barnet Woolf for advice on the statistical analysis, and Professor R. W. B. Ellis for his constant help and encouragement.

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AN ANTHROPOMETRIC STUDY OF PREMATURELY BORN CHILDREN AT THE AGE OF 5 YEARS

BY

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A considerable number of growth studies on prematurely born children have been carried out since 1919 when Ylppö (1920) published the first major report on this subject (Capper, 1928; Hess, Mohr and Bartelme, 1934; von Sydow, 1936; Illingworth, 1939; Brander, 1941; Levine and Gordon, 1942; Asher, 1946; Drillien, 1948; Alm, 1953; Douglas and Mogford, 1953). The earlier results are unreliable and contradictory, but later workers agree in general that premature infants remain a little below average in height and weight. With a steady increase in survival rate the characteristics of this group of children are likely to alter. In addition, racial, economic and other factors have an important bearing on growth pattern. Therefore as there are no detailed anthropometric data on Scottish children born prematurely the present investigation was undertaken.

Material

This paper presents the results of an anthropometric study of children born prematurely (birth weight 2·5 kg. or less) in Glasgow Royal Maternity and Women's Hospital in 1949. Children with a birth weight over 2·5 kg. born in the same hospital in the same year were used as controls. The period during which measurements were made extended from September, 1954, until May, 1955.

Of the infants delivered prematurely in 1949, 316 left hospital. Details of their subsequent history are as follows:

Died after discharge	19
Emigrated	9
Removed from Glasgow (traced)	33
Removed from Glasgow (not traced)	32
Adopted	4
Visited but uncooperative	2
Attended for measurement	217
Total	316

Thus, 217 or 68·7% of the original sample of premature infants were measured. This figure compares favourably with that of other studies and seems as high as it is possible to reach without a large team of workers. Although those who were measured cannot be regarded as entirely representative, there is no evidence that the sample measured would differ significantly from the whole group.

To obtain a control group an attempt was made to trace each fifth mature child dismissed from hospital at the same period. As in the premature group a proportion could not be traced so the next fifth child on the list was chosen and so on until an equal number was obtained. A few from 1950 were taken towards the end of the survey to reach the required total. The number, birth weight and sex of the children in each group is shown in Table 1.

TABLE 1
BIRTH WEIGHT AND SEX DISTRIBUTION OF CHILDREN

Premature			Mature		
Birth Weight	M	F	Birth Weight	M	F
2 lb. –2 lb. 8 oz. (0·91–1·13 kg.)	1	—	5 lb. 9 oz.–6 lb. (2·52–2·72 kg.)	11	11
2 lb. 9 oz.–3 lb. (1·16–1·36 kg.)	2	1	6 lb. 1 oz.–6 lb. 8 oz. (2·75–2·95 kg.)	12	17
3 lb. 1 oz.–3 lb. 8 oz. (1·39–1·59 kg.)	5	5	6 lb. 9 oz.–7 lb. (2·98–3·17 kg.)	18	21
3 lb. 9 oz.–4 lb. (1·62–1·81 kg.)	8	6	7 lb. 1 oz.–7 lb. 8 oz. (3·2–3·41 kg.)	17	21
4 lb. 1 oz.–4 lb. 8 oz. (1·84–2·04 kg.)	25	22	7 lb. 9 oz.–8 lb. (3·43–3·63 kg.)	19	16
4 lb. 9 oz.–5 lb. (2·07–2·27 kg.)	27	32	8 lb. 1 oz.–8 lb. 8 oz. (3·66–3.86 kg.)	18	10
5 lb. 1 oz.–5 lb. 8 oz. (2·30–2·50 kg.)	37	46	8 lb. 9 oz.–9 lb. (3·88–4.08 kg.)	11	3
			9 lb. 1 oz.–9 lb. 8 oz. (4·11–4·31 kg.)	4	6
			9 lb. 9 oz.–10 lb. (4·34–4·54 kg.)	4	2
			Over 10 lb. (>4·54 kg.)	—	1
Totals	105	112		114	108

Methods

The survey was undertaken with the help of a health visitor seconded from Glasgow Corporation Public Health Department. The procedure was essentially the same in both groups of children. The health visitor tried to trace each infant and visit the home. She then invited the mother to attend

the Royal Hospital for Sick Children with her child for measurement. At the same time information was obtained of the child's past history, of the socio-economic conditions and other details of the home situation. It is of interest that only 24% of the mothers of prematures gave the correct birth weight as compared with 37% of the mothers of the mature infants.

The tracing of these children was rendered extraordinarily difficult by the remarkable shift of population to new housing estates which occurred in Glasgow in this post-war period. Approximately one-third of the children were not traceable at the 1949 address. The frequency with which they moved house was also extraordinary, five removals within five years being not infrequent. The assistance of the Public Health Department, Local Executive Council, school attendance officers and many others was invoked and proved very useful. We would thank them for their services.

It became apparent early in the investigation that it was going to be impossible to have each child attend hospital on or near the fifth birthday. As we were anxious to obtain measurements of as many of the original prematures as possible we had therefore to forego this.

In 40 cases the parents, though agreeable to having their children measured, could not or would not bring them to hospital. This was overcome by visiting them at school and measuring them there.

Comparability of the Premature and Mature Groups

Without resorting to pairing it was felt that both groups should be comparable as far as socio-economic factors are concerned as the patients delivered in Glasgow Maternity Hospital tend to be of a rather homogeneous and poor socio-economic group. The two groups were subsequently studied with regard to housing, social class, maternal age and birth order, factors which have a bearing on birth weight and subsequent growth. Details are presented in Tables 2, 3, 4 and 5. These show that

TABLE 2
BIRTH ORDER OF CHILDREN MEASURED

Birth Order	Premature	Mature
1st	84	84
2nd	56	62
3rd	18	24
4th	23	22
5th	16	13
6th	4	3
7th	2	4
8th	4	4
9th +	9	6
Unknown	1	—
Total	217	222

TABLE 3
AGE OF MOTHER AT BIRTH

	Premature	Mature
20 years and under	12	15
21–25 years	54	52
26–30 years	52	64
31–35 years	50	37
36–40 years	34	42
41 years and over	14	12
Unknown	1	—
Total	217	222

TABLE 4
SOCIAL CLASS

Social Class	Premature	Mature
I	1	—
II	28	25
III	84	112
IV	26	19
V	73	63
Unclassified	5	3
Total	217	222

TABLE 5
HOUSING

Inmates per Room		Premature	Mature
	0·4	1	—
	0·5	1	—
	0·75	6	3
	0·8	1	—
	1·0	18	23
	1·14	1	—
	1·25	14	7
	1·33	15	21
	1·4	1	—
	1·5	35	55
	1·6	1	—
	1·67	14	8
	1·75	6	—
	2	26	21
	2·25	2	3
	2·33	3	4
	2·5	3	13
	2·67	2	1
Over-crowded	3	37	43
	3·5	—	4
	4	18	12
	4·5	1	1
	5	4	2
	5·5	2	1
	6	1	—
	7	3	—

with regard to birth order there is no difference between the two groups. Forty-seven per cent. of the prematures and 47·3% of the controls came from overcrowded houses (two or more inmates per room), though more prematures came from very bad or very good homes. Slightly more prematures came from social classes IV and V, whereas approximately half the matures came from social class III. This difference is just significant. The illegitimacy rate was 5·0% in the premature group and 2·2% in

the control, such a low rate as not to affect the comparability of the groups. It is clear therefore that apart from a slight difference in social class the two groups are comparable.

Measurements Undertaken

Six body measurements were selected from those used in the Harpenden Growth Survey (Tanner, 1955), namely height, weight, sitting height, biacromial diameter, bi-iliac diameter and subcutaneous fold thickness. One operator (H.V.) undertook all the height and weight measurements, while the other (A.L.S.) undertook the rest, an arrangement which was maintained throughout the survey.

The same instruments were used throughout, except in the case of 40 children in the premature group who had to be visited in school in order to obtain their measurements. In this instance the heights and weights were recorded from the local authority school instruments. The weighing machines were of standard lever type.

Height, Weight and Sitting Height. These were all measured according to the method described in a standard textbook (Nelson, 1954). All children were weighed naked. Height and sitting height were measured to within 0·25 cm. and weight to within 50 g.

Subcutaneous Fold Thickness. As changes in fold thickness at one site are representative of changes over the rest of the body (Edwards, 1950; Hammond, 1955a) only one site was studied. Of the areas recommended by Tanner (1955) that just below the angle of the left scapula was selected. The Harpenden Growth Study (or M.R.C.) calipers, with plate sizes 6 × 15 mm. and pressure 10 g./mm.^{2}, were used. A certain amount of 'drift' occurred if pressure was maintained, due to squeezing of the tissue. After some experience a relatively standard period of pressure (which avoided much squeezing) was used throughout. The reading on the dial gauge was taken to 0·1 mm.

Biacromial and Bi-iliac Diameters. These were taken with sliding calipers which were guided into the correct position by extending the fingers along the arms of the calipers and feeling for the bony prominences which, in this instance, were the most lateral points of the acromion processes and the most lateral points of the iliac crests. These were taken with the child standing erect with arms to the sides and were recorded to the nearest 0·1 cm.

Duplicate and sometimes triplicate measurements were taken in a proportion of cases to see how far the figures obtained were repeatable. For inclusion in the final figures a mean of the readings was used.

Accuracy of Certain Measurements

Height and weight can be measured with a fair degree of accuracy, but this is not likely to be so in the case of certain of the other measurements undertaken. Biacromial diameter is very easily varied by a child's tendency to shrug his shoulders or shrink when calipers are placed across them, a tendency which is difficult to overcome completely in many children. It is also difficult to standardize the period for which the skin-fold calipers are applied; maintenance of pressure results in erroneously low readings. In addition, slight variations in the site of application below the angle of the scapula can produce surprising variation in the figures obtained.

The best measure of reliability is given by the coefficients of variation from repeated measurements taken during one examination. The results in the 180 cases in which this was done are as follows:

	Subcutaneous Fold Thickness	Biacromial Diameter	Bi-iliac Diameter
Coefficient of variation ..	3·6%	0·92%	0·65%

A coefficient of variation of 1% is very satisfactory. It roughly means that the true value corresponding to an observed value will lie within ±2% of the observed value. The coefficient of variation of 3·6% associated with fold thickness is rather too high, though is still satisfactory.

Results

The ages of the premature children ranged from 4 years 9 months to 6 years 2 months and of the mature children from 4 years 3 months to 6 years. Before the differences in weight, etc., could be examined it was necessary to adjust the measures to a standard age. The male premature children had a mean age of 5 years 6·1 months and the male mature a mean age of 5 years 3·2 months. To reduce the errors of estimate the measures of weight, etc., were adjusted to the age of 5 years 4·6 months, which is the mean age of all male (premature and mature) children. Similarly, the measures of the female children were adjusted to the age of 5 years 4·4 months. To make these adjustments the average rate of increase (or decrease) was determined for all males and females separately by the use of linear regression equations for each of the

variables (weight, height, etc.) and multiplied by the difference in age between the actual and the standard ages; this product was then subtracted from the actual weight or height, etc., of the child. In practice the adjustment was made only to the mean values. Thus, for example, the linear regression of weight on age for male children gave an average growth of 0·904 kg. per year and the adjusted mean weight for premature males

= actual mean weight—0·904 (5·506—5·383)
= 17·666—0·904 (+0·123)
= 17·555 kg. = 17·56 kg.

where the mean age of all premature males is 5·506 years, and the mean age of all (mature and premature) males is 5·383 years.

The results of this statistical analysis are presented in Table 6.

TABLE 6
MEAN VALUES OF MEASUREMENTS IN PREMATURE AND MATURE GROUPS

	Mean Values			
	Males Adjusted to Age 5 yr. 4·6 mth.		Females Adjusted to Age 5 yr. 4·4 mth.	
	Premature	Mature	Premature	Mature
Weight (kg.)	17·56*	18·73	16·74*	18·19
Height (cm.)	106·22*	108·00	104·69*	107·32
Sitting height (cm.) ..	61·07	61·58	59·96*	60·99
Subcutaneous fold thickness (mm.)	5·52	4·96	5·55	5·67
Bi-iliac diameter (cm.) ..	17·74*	18·10	17·39*	17·77
Biacromial diameter (cm.)	23·57*	24·04	23·00*	23·69

* Denotes significant differences between premature and mature children.

Discussion

The results indicate that the height, weight and breadth of children born prematurely in Glasgow in 1949 were less than in a comparable group of full-term children aged 5 years. The differences are statistically significant in both sexes and for each measurement except for sitting height in males. With respect to height and weight these results are in agreement with recent work. The findings for sitting height and bi-iliac (intercristal) diameter are in agreement with those of Hess *et al.* (1934) in the United States.

The subcutaneous fold thickness is unique in that there is no significant difference between the mature and premature groups. This is not surprising as subcutaneous fat normally decreases in thickness until the ages of 5 or 6 years, whereas other measurements increase with age (Stuart and Sobel, 1946; Hammond, 1955b). The figures found by Hammond for a group of 5-year-old children are similar to those found in the mature children in this series:

	Subcutaneous Fold Thickness at Subscapular Site (mm.)	
	Males	Females
Glasgow mature group ..	4·96	5·67
Hammond (1955b) ..	4·97	5·18

It is apparent that girls are fatter than boys, though this difference is negligible in the premature children.

A comparison of the figures for the mature group with those from other centres is also of interest. The weight and biacromial diameters of a representative sample of Edinburgh schoolchildren aged 5 + years as reported by Provis and Ellis (1955) are in each instance very similar but slightly greater than those for the mature Glasgow children aged 5 years 4 months.

	Glasgow		Edinburgh	
	Male	Female	Male	Female
Weight (kg.)	18·73	18·19	19·01	18·9
Biacromial diameter (cm.) ..	24·04	23·69	24·47	24·72

The difference is probably mainly due to the fact that the Glasgow children come from a poorer socio-economic group. This is confirmed by a further comparison with Hammond's (1953) figures for schoolchildren in the north of England which show that height, weight, sitting height and biacromial diameter in the mature Glasgow group are all very much more closely related to those measurements in children from council schools (poor districts) as opposed to independent schools. Hammond's (1955a) latest figures for an average sample of Leeds' children are mid-way between (Table 7).

TABLE 7
COMPARISON BETWEEN MATURE CHILDREN AND OTHER GROUPS OF 5 YEARS OLD REPORTED BY HAMMOND (1953 AND 1955a)

	Weight (kg.)		Height (in.)		Sitting Height (in.)		Biacromial Diameter (in.)	
	M	F	M	F	M	F	M	F
Glasgow—mature group	18·73	18·19	108·0	107·32	61·58	60·99	24·04	23·69
Average Leeds children ..	18·69	19·02	110·0	110·3	62·3	62·1	24·3	24·2
Independent schoolchildren ..	20·9	19·4	115·2	113·7	65·6	63·8	24·7	24·3
Council schoolchildren	18·45	18·41	108·0	107·8	61·4	60·5	23·3	23·2

There seems to be disagreement between various reports as to whether boys at this age have broader shoulders than girls. Thus Provis and Ellis (1955) and Hogben, Waterhouse and Hogben (1948) found the mean shoulder width of the girls to be greater than the boys', whereas the reverse was found by Hammond (1953) and in this series. The differences are, however, slight and could result from the less satisfactory nature of this measurement already mentioned.

Because of the age range of the children under survey it was possible to calculate apparent rates of growth for each of the four main groups of children. These showed no significant difference between the mature males, the premature males and the premature females. For some reason which is not clear the mature females had an apparently greater growth rate in most of the features studied throughout the age range. These figures have, however, not been published as they were derived from a cross-sectional and not a longitudinal study.

Summary

The present paper reports the results of a cross-sectional anthropometric study on 217 prematurely born and 222 full-term Glasgow children aged 5 years.

The two groups were analysed with regard to factors which have a bearing on subsequent growth and were found to be similar except for a slight bias towards poorer social class in the premature group.

Six measurements were recorded, namely, height, weight, sitting height, subcutaneous fold thickness, biacromial diameter and bi-iliac diameter.

With the exception of subcutaneous fold thickness in boys and girls and sitting height in boys the measurements for the mature children were significantly greater than those for the premature when the series are compared separately.

Certain measurements were compared with those in other series and in general the results found to be similar.

I wish to record my sincere thanks to Professor Stanley Graham for his guidance and help, to Dr. R. A. Robb of the Department of Statistics, Glasgow University, for his extensive statistical analysis, and to Miss Marshall, lately health visitor with Glasgow Corporation, for her tireless efforts in tracing these children and helping with the survey.

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AGLOSSIA CONGENITA

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CINERADIOGRAPHIC FINDINGS

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Aglossia may be either congenital or acquired. Only congenital aglossia is considered in this paper. The principal features of the reported cases are summarized in the table.

In 1932 Rosenthal recorded a case of aglossia, and in a review of the literature found three previously reported cases. He cites de Jussieu who, in 1718, reported a Portuguese girl of 15, who in the floor of her mouth had a tiny wart-like elevation which was muscular and could be moved. She could talk easily and clearly in French except for certain sounds. Chewing was difficult and she used her fingers to move the food in her mouth. Fluids were swallowed easily if she leaned forward and only took small amounts; solids were more difficult. The sense of taste was unimpaired.

Spiller (1816) described a child with a shallow elevation across the floor of the mouth, in the region of the root of the tongue, which contracted on crying. The soft palate was absent except for two lateral rudiments.

Kettner (1907) reported a boy of 4 years who had a small triangular mass where the body of the tongue normally arises. In the floor of the mouth there were also two antero-posterior ridges which could be made almost to fill the space between the teeth. The palate was completely cleft and there was no sign of the band between the tongue and palate which had been divided at birth. There were also severe abnormalities of the hands and feet. The right foot consisted of a heel and a soft ridge replacing the metatarsus. The left foot had only a rudimentary heel. The index and middle fingers of both hands were absent and the other fingers were deformed except for the right fifth finger. The boy pronounced his letters well except for d and t.

Rosenthal's case was a 3-year-old girl, the third child of healthy parents, with no family history of congenital abnormalities. Pregnancy and delivery had been normal. The face had a retruding lower jaw, a narrow chin and a rudimentary median cleft of the lower lip. The tongue consisted of a small notched median rudiment in the anterior part of the floor of the mouth. A hypertrophic ridge of mucous membrane extended along the lower edge of the left mandible, covering the left parotid duct. A hypertrophic sublingual ridge was capable of some movement and simulated part of the tongue. The tonsils were large and divided into upper and lower lobes. These came together on crying and apparently on swallowing, almost closing off the oral cavity posteriorly. The teeth were irregular and some were missing. The child had no difficulty in talking and in making herself understood, although speech was not clear. There was a moderate and continuous drooling and she found it difficult to swallow solids without the help of the fingers. The right hand was represented by a thumb which consisted of two bones; all the carpals were smaller than normal. A rudimentary fifth metacarpal was present. The wrist, third, fourth and fifth fingers of the left hand were normal but the thumb was underdeveloped and the index finger had a rudimentary second and no terminal phalanx. The right foot had a normal calcaneus and talus, but all the other bones were lacking except for a rudimentary phalanx of the first toe. The left foot was normal. The child walked normally and used her hands well.

Watkin (1925) reported a girl with a narrow face and small lower jaw. The anterior two-thirds of the tongue were missing but there was a hypertrophied sublingual gland. The posterior one-third was rudimentary. The permanent dentition was not complete in either jaw. The viscera, including dextrocardia, were transposed. Speech was good,

the t and th sounds were normal, but she could not 'hiss' as in c, s and x.

Sinclair and McKay (1945) published a post-mortem report of a female child of 4 weeks. The facial features were normal except for an upper median hare-lip. The anterior two-thirds of the tongue was missing and a bifid posterior stump projected from the floor of the mouth. The hard and soft palates were represented by ridges on the medial aspects of the upper jaw. The teeth, larynx and nerves were normal. The first cervical vertebra was compressed and there was a small heart. All the fingers were short and webbed, as were three toes of each foot.

Farrington (1947) reported a man of 23 years with a sharp narrow and receding lower jaw. There was no tongue. At birth a fibrous band had passed between the hard palate and the floor of the mouth but it had been divided and no sign of it remained. The submandibular and sublingual glands were hypertrophied and the sublingual ridges were prominent and appeared hypertrophied. The palate was normal. The deciduous dentition had been normal, but the permanent teeth were irregular and decayed early. He talked fairly normally but pronounced q as in 'to'. Chewing and swallowing were performed satisfactorily, the fingers being used. The sense of taste was normal.

Fitzwilliam (1927) quotes de Jussieu and Kettner's cases and the following, but without giving references:

> 'Blumenbach saw a person without a tongue and whose sense of taste was perfect.
>
> Moncorvo saw a case with complete congenital absence of the tongue.
>
> Filho saw a 10-day-old male with a badly developed jaw and a small elevation in the floor of the mouth representing the tongue. The tonsils and soft palate were missing and ossification of the head defective. The baby could not feed properly.
>
> Griffiths saw a premature male in whom there was a gross deformity of the lower jaw, absent tongue and cleft hard palate.
>
> Maygrier and Haller saw a patient in whom the tongue was represented by a small mass in the floor of the mouth. Other deformities were present.'

Case History

J.W., a boy, aged 5 weeks, was admitted to hospital because he had not been taking his feeds well and had lost weight.

The mother, a primipara, lost a little weight at the beginning of the pregnancy and a mild toxaemia developed during the last two months, but there were no infectious diseases.

Labour was uneventful and resulted in the birth of a full-term baby (5 lb. 12 oz.) who cried lustily. The only abnormality noticed at the time was webbing of the fingers of the left hand (Fig. 1). When breast feeding was started on the third day it was found that the baby did not feed properly and an abnormality of the tongue was then noticed. Bottle feeding was begun but the baby still had difficulty in feeding, requiring an hour to take 3 oz. He thrived and put on weight steadily until

FIG. 1.—J.W., aged 4 months, showing the syndactyly of the left hand.

the week before admission when he fed poorly and lost some weight.

Examination on admission showed a fairly well nourished baby with a receding lower jaw (Fig. 2). The vestibular mucosa was directly continuous with that of the floor of the mouth as the anterior alveolar margin of the mandibles was depressed. The mucosa of the floor of the mouth was filiform and appeared to consist

FIG. 2.—J.W., aged 4 months, showing the receding lower jaw.

of normal tongue mucosa, but there was no tongue (Fig. 3). Laterally this mucosa was raised into two ridges which ran alongside and parallel with the medial borders of the mandibles. These folds probably contained muscle as they moved when the baby cried. In the midline of the posterior part of the floor of the mouth, and visible only on crying, there was a mobile pyramidal projection about ½ cm. in height. The hard and soft palates, uvula, tonsils and larynx were normal. The mouth was infected with *Oidium albicans*.

The only other abnormality was syndactyly of the left hand. The left thumb was normal, the second and third digits were completely joined, the third and fourth were webbed to the proximal interphalangeal joint and the fourth and fifth were webbed to the distal interphalangeal joint.

FIG. 3.—J.W., aged 4 months, showing the lateral folds in the floor of the mouth and the depressed alveolar margins of the mandibles anteriorly.

The baby fed slowly from a bottle using a soft teat with a large hole, but swallowed without choking or coughing and there was no nasal regurgitation. He breathed and cried normally.

Radiographs showed three tooth buds in each mandible and a normal bony structure of the hands and feet. There was no transposition of the viscera or dextrocardia. The oral infection with *Oidium albicans* responded to treatment with gentian violet and the baby started to gain weight.

After discharge from hospital the baby continued to thrive and his rate of feeding improved. At 3 months he was feeding normally. The baby is now 10 months old and has had no further feeding trouble. He has no teeth, but takes most minced and sieved foods when fed with a spoon or cup; he appears to discriminate taste. Food which is stuck to the hard palate is dislodged with the fingers. He says 'Mum' and 'Dad'. The submandibular gland now appears a little hypertrophied and the sublingual ridges are well marked.

Cineradiographic Investigations

Cineradiographs were taken at 25 frames per second with an image intensifier. Three films each of four seconds' duration were obtained.

At the first examination at 6 months of age the child was given a mixture of milk and barium suspension in a bottle supplied by the mother. When the bottle was inverted the mixture dripped slowly from the teat. The teat was adjusted in position in the mouth (Fig. 4). Jaw movements began. When the mandible was lowered the teat distended with barium; the lips formed a seal round the base of the teat; the floor of the mouth was raised above the position of rest and applied to the lower surface of the teat, the upper surface of the teat being apposed to the hard palate. The posterior part of the soft palate was thickened and drawn forwards to meet what seemed to be a normal posterior part of the tongue. No free or anterior portion of the tongue was recognized. A small collection of the contrast medium occupied the space between the end of the teat and the soft palate. The larynx and pharynx were air filled and in communication with the nose; they appeared normal. As the lower jaw was raised the floor of the mouth was lifted higher and the teat was narrowed and displaced forwards; the soft palate reverted to the appearance normally seen at rest, then moved backwards and slightly upwards towards the posterior wall. Palato-glossal closure was maintained by elevating the posterior portion of the tongue against the soft palate. These actions resulted in an increase in the size of the pool of contrast medium in the mouth. Two or three repeated jaw movements seemed to be necessary to obtain a sufficiently large bolus. The tongue and soft palate then separated and the bolus flowed into the pharynx. The back of the tongue was then applied to the soft palate from before backwards and the bolus expressed into the pharynx and swallowed. The movement of the bolus through the pharynx seemed to be entirely normal. As the bolus was expressed from between the posterior part of the tongue and the soft palate, the mandible was lowered to allow the teat to re-fill.

At the second examination at 10 months the child was given barium suspension by teaspoon while sitting up (Fig. 5). Cineradiographs showed that fluid flowed off the spoon into the child's mouth and over the dorsal surface of the tongue into the valleculae, some spilt over the edge of the epiglottis. When a considerable quantity of the barium had

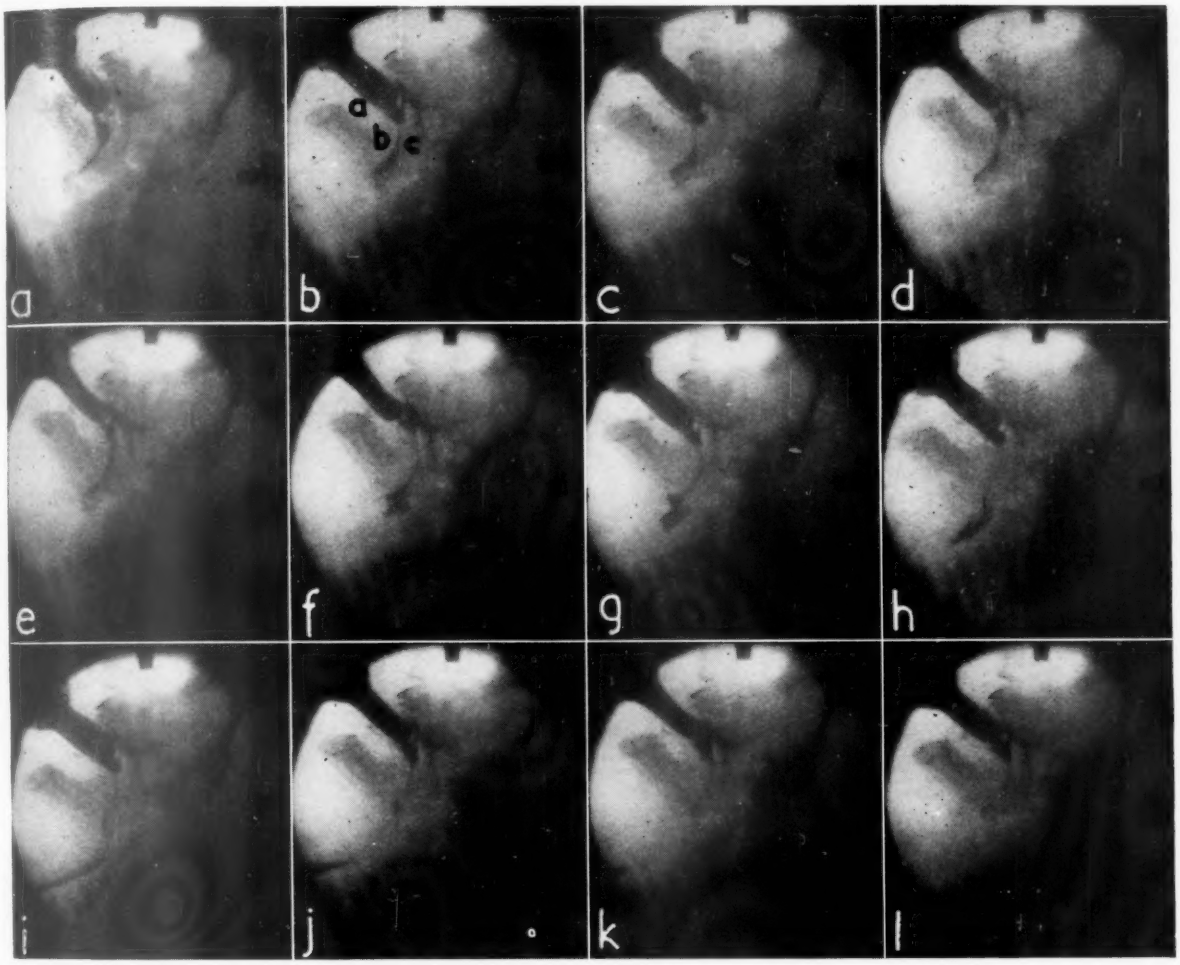

FIG. 4.—*A selected series of cineradiographs from an examination of J.W. at 6 months while being fed with barium sulphate and milk from a bottle.*

(*a*) Position of the floor of the mouth at rest.

(*b*) Diagram of Fig. 4 (*c*). (a) floor of the mouth.
(b) posterior part of the tongue.
(c) soft palate.

(*c*) The teat is in position in the mouth. The soft palate is thickened and drawn forwards to make contact with what seems to be a normal posterior part of the tongue thus establishing palato-glossal closure in the normal manner. The floor of the mouth is raised and apposed to the lower surface of the teat. A small quantity of barium suspension is held close to the end of the teat and there is a thin line of barium in the line of the palato-glossal closure; at a lower level a further small quantity of barium suspension is held between the posterior pillars and the tongue just above the valleculae in front of the tonsils.

(*d*) A further quantity of the barium has been drawn into the mouth. The teat is slightly narrowed and the tongue and soft palate are parting.

(*e*) Palato-glossal closure is no longer maintained. Barium spills downwards.

(*f*) The posterior part of the tongue is raised against the soft palate; a quantity of barium has been displaced into the pharynx. The naso-pharynx is closed by apposition between the soft palate and the posterior pharyngeal wall.

(*g*) The barium is displaced downwards in the pharynx. The soft palate is down and closely apposed to the dorsal surface of the tongue. Nasopharyngeal closure is maintained by forward movement of the upper posterior pharyngeal wall.

(*h*) Further displacement of the bolus with bowing forwards of the upper posterior pharyngeal wall.

(*i*) and (*j*) The bolus passing through the lower pharynx into the oesophagus.

(*k*) Further displacement of the bolus downwards. Air is entering the pharynx.

(*l*) The airway is re-established.

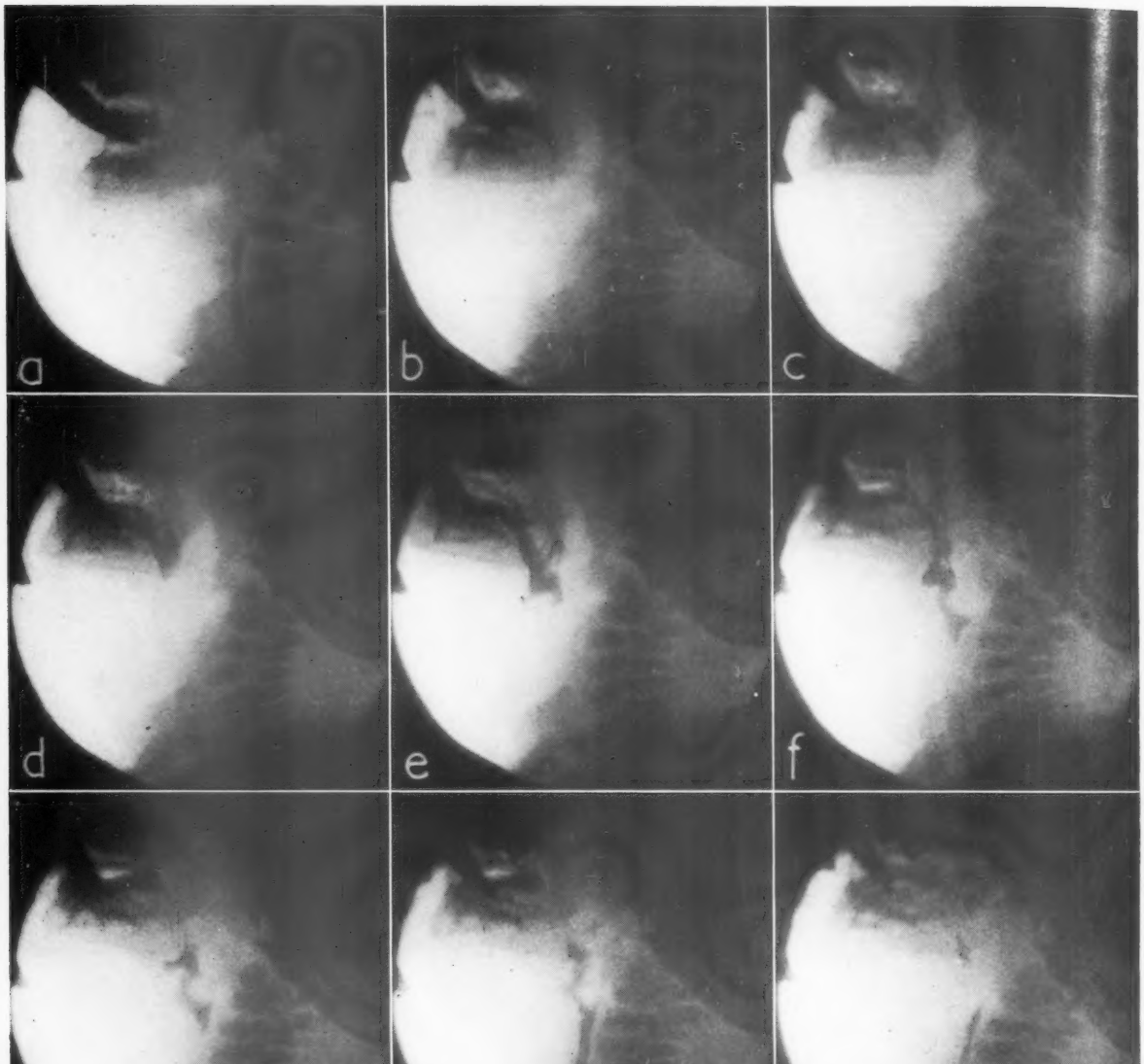

FIG. 5.—*The child sitting erect taking barium suspension from a spoon. A series of prints from the cineradiographic examination at 10 months.*

(*a*) Barium taken into the mouth from the bowl of the spoon; the floor of the mouth is raised from the position of rest. Palato-glossal closure maintained between the soft palate and the posterior part of the tongue. The barium in the oesophagus is part of a previous bolus.

(*b*) The head is being extended. Note the position of the chin and compare it with the position shown in Fig. 5 (*a*). The soft palate and the tongue have parted to allow the barium to flow down to the level of the tonsils; the floor of the mouth and the posterior part of the tongue have been lowered.

(*c*) and (*d*). Further extension of the head. Barium held up at the level of the tonsils.

(*e*), (*f*) and (*g*). Barium descending through the pharynx in the normal manner. The back of the tongue has arched backwards (Fig 5 (*f*)) and the posterior pharyngeal wall has been brought forwards so that the cavity of the upper pharynx is obliterated and the soft palate apposed to the dorsum of the tongue.

(*h*) Most of the contents of the pharynx expressed into the oesophagus.

(*i*) A trace of barium remains upon the upper surface of the epiglottis. Pharyngeal cavity obliterated.

collected in the pharynx the posterior portion of the tongue was elevated against the soft palate, cutting off the barium in the pharynx from the contents of the mouth. This action was then continued as a normal swallowing movement, the contents of the pharynx being expressed into the oesophagus. When the airway was re-established, the child tilted the chin a little upwards and parted the tongue and soft palate; the posterior portion of the tongue was moved forwards, its arched dorsal surface being flattened to form a steep slope allowing a further quantity of barium to flow into the valleculae; the soft palate at this stage was straight and not appreciably elevated. The action described above was then repeated. Two more swallowing movements were needed to take the bulk of one teaspoonful. Before the last swallowing movement the child extended the head to the maximum degree, apparently in an attempt to empty the mouth, and as this movement was taking place there was some elevation of the floor of the mouth towards the hard palate; the changes in the contour of the floor of the mouth suggested that there might be some contraction of the fibres of the tongue musculature. When swallowing movements were concluded the residuum left in the forepart of the mouth was considerably greater than the amount which would be left in the normal child. The films taken in the antero-posterior projection showed that the bolus of barium passed into the pharynx over the midline of the dorsal part of the tongue. Another film in the lateral projection, with the child lying on its back, showed that the method of swallowing was similar to that described in the sitting position, except that the child did not have to extend the chin so far in order to clear the mouth.

In normal babies the tip of the tongue is thrust upwards against the upper gum and the forepart of the tongue is applied to the teat from before backwards, so tending to express the contents of the teat and displace the bolus backwards into the mouth (Ardran and Kemp 1955). In this patient the flow of barium from the teat into the mouth appeared to be brought about by three separate factors. First, by drips from the teat under the influence of gravity. Secondly, by suction when the jaw and the floor of the mouth were depressed and thirdly, by compression of the teat by elevation of the floor of the mouth. The last factor was probably the least effective as it was not accompanied by occlusion of the neck of the teat, since contents of the teat would be more readily displaced into the bottle through the wide open neck of the teat rather than onwards through the much smaller opening at the tip of the teat.

The behaviour of the floor of the mouth at the second examination strongly suggests that there are some fibres of the tongue present in this situation, possibly in the two lateral ridges, which have been described clinically.

Embryology

According to Baxter (1953) the floor of the mouth in the early embryo consists of six pharyngeal arches separated by pharyngeal grooves. Ventrally the first and second arches meet their fellows in the midline and at the point of fusion of the first (mandibular) arches a small median swelling, the tuberculum impar, appears before the fourth week. A larger midline swelling, the hypobranchial eminence, appears between the third, fourth and fifth arches.

Embryologically the tongue consists of anterior and posterior parts. The anterior part first appears as the tuberculum impar, but at the fifth week elevations of the first arches arise on each side of it. Later, after the seventh week, they fuse with the tuberculum impar and with each other to form the anterior two-thirds of the tongue.

The posterior one-third is formed by the third arch mesoderm, which grows forward as a V-shaped process from the anterior part of the hypobranchial eminence, burying the second arch. The line of fusion of the anterior and posterior parts is V-shaped and is indicated in the adult tongue by the vallate papillae. The posterior part of the hypobranchial eminence forms the epiglottis.

These swellings from the first and third arches form the mucous membrane, mucous glands, lymphoid and connective tissues. The muscle is formed by three or four occipital myotomes which migrate ventrally bringing with them their own nerve supply, the hypoglossal nerve.

Discussion

The embryological formation of the tongue is a complex process and in all these patients it appears to have been interrupted at an early stage. The anterior part of the tongue is absent and the posterior part is represented by a rudiment. In one case the posterior median rudiment was bifid, suggesting that it has been formed from the hypobranchial eminence and not from the tuberculum impar. The epiglottis, which is also formed from the hypobranchial eminence has been present in all cases. The failure of formation of the tongue is, therefore, most commonly due to an agenesis of the first mandibular arch. In every reported case the rudiments of the tongue, when present, were mobile and, therefore, contained innervated muscle. Thus the

TABLE

CLINICAL FEATURES OF PUBLISHED CASES

	Farrington (1947)	Sinclair (1945)	Rosenthal (1932)	Watkin (1925)	Kettner (1907)	Spiller (1816)	de Jussieu (1718)	Blumen-bach	Moncorvo	Filho	Griffiths	Maygrier and Haller	Ardran and Kemp (1955)
Sex	Male	Female	Female	Female	Male	—	Female	—	—	Male	Male	—	Male
Age	23 yr.	4 weeks	3 yr.		4 yr.	Child	15 yr.			10 days	Premature		10 mth.
Facial features ..	Sharp, narrow	Normal	Narrow	Narrow	—	—	—	—	—	—	—	—	Narrow
Lower jaw ..	Receding	Normal	Receding	Receding	—	—	—	—	—	Badly developed	Gross deformity	—	Receding
Hare lip ..	Absent	Median upper	Median lower	Absent	—	—	—	—	—	—	—	—	Absent
Cleft palate ..	Absent	Complete	Absent	Absent	Complete	Soft palate	—	—	—	Complete	Hard palate	—	Absent
Teeth	Irregular	Normal	Irregular	Irregular	—	—	—	—	—	—	—	—	—
Glands													
Submaxillary ..	Hypertrophied	Normal	Normal	Normal	—	—	—	—	—	—	—	—	Hypertrophied
Sublingual ..	Hypertrophied	Normal	Hypertrophied	Hypertrophied	—	—	—	—	—	—	—	—	Hypertrophied
Chewing	Good	Died from marasmus	—	—	—	—	Some difficulty	—	—	Could not suck	—	—	Some difficulty
Swallowing ..	Good	—	Fair	—	—	—	Some difficulty	—	—	—	—	—	Some difficulty
Speech	Good	—	Fair	Good	Good	—	Good	—	—	—	—	—	—
Taste	Normal	—	—	—	—	—	Normal	Normal	—	—	—	—	Normal
Intra-oral band	Present	—	—	—	Present	—	—	—	—	—	—	—	Absent
Digits	Normal	Syndactyly	Adactyly	Normal	Adactyly	—	Normal	—	—	—	—	—	Syndactyly
Tongue													
Anterior ..	Absent	Absent	Small notched median rudiment	Absent	Two anterior posterior ridges	Absent	Wart-like elevation in floor of mouth	Absent	Absent	Small elevation in floor of mouth	Absent	Small mass in floor of mouth	Two antero-posterior ridges
Posterior ..	Absent	Bifid posterior stump	Absent	Rudimentary	Small triangular mass	Shallow elevation		Absent	Absent		Absent		Normal

occipital somites, and their nerves, migrate normally, but because of the previous agenesis of the first arch they cannot form the normal musculature. This view is confirmed by Sinclair's case which was dissected and found to have a normal hypoglossal nerve.

Some malformation apart from the aglossia is always found, and may be either associated with the branchial arches or apparently unrelated.

The face is usually sharp and narrow with a receding chin, the appearance being described as 'bird-like'. This is due to a hypoplasia of the mandible and a narrow mandibular arch. A median hare-lip occurred in two cases, once of the upper and once of the lower lip; a cleft palate was present in four cases, three times complete and once of the soft palate only. The mandibular teeth, especially the permanent dentition, are usually irregular and of poor quality. An intra-oral band, between the floor of the mouth and the palate, was divided at birth in two cases; this was probably the remains of the bucco-pharyngeal membrane.

The other deformities which have been described mainly affect the digits. Two cases had adactyly and one syndactyly; the present case has syndactyly. Transposition of the viscera with dextrocardia occurred once. The frequency with which aglossia is accompanied by digital deformity is striking; its explanation is obscure. Since the tongue completes its development before the hard palate appears it is unlikely that a single noxious influence can be responsible and it is more likely that the association is determined genetically.

The disability caused by the aglossia is not very great. It was found that the baby had to be bottle-fed, using a long soft teat with a large hole. The reason for this was shown by the radiographic investigation. In normal babies the tip of the tongue is thrust upwards against the upper gum, closing the neck of the teat, then the forepart of the tongue is applied from before backwards compressing the teat against the hard palate, thus expressing the contents of the teat into the mouth.

The baby with aglossia is unable to perform these actions and milk enters the mouth under the influence of gravity, through the large hole in the teat. This is assisted by suction and compression of the teat performed by a raising and lowering of the floor of the mouth. Compression cannot be very effective as there is no closure of the teat and the floor of the mouth cannot be brought into apposition with the hard palate. Three patients showed hypertrophy of the structures in the anterior part of the floor of the mouth and this appears to have started in the present case by the tenth month. This hypertrophy increases the effectiveness with which the floor of the mouth can be raised against the hard palate during the compression movement and thus partially compensates for the aglossia. Once the food has left the mouth the posterior part of the tongue functions normally; the bolus is swallowed in the normal manner which explains why there is no nasal regurgitation, choking or coughing.

The sense of taste was normal in the two adult cases and the present case appears to differentiate tastes. These children are slow in learning to talk, but they later speak without difficulty and are easily understood, although there are always some sounds which are not properly formed.

Summary

A case of aglossia congenita in a baby is reported.

Twelve previously reported cases are reviewed. The embryological formation of the tongue is considered. Investigation by cineradiography shows the way in which the baby feeds and swallows. No cause for the deformity has been found. The disability caused by aglossia congenita is not very great after the first three months.

We wish to thank Dr. A. C. Kendall for his permission to publish this case, and for his advice during the preparation.

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THE DIAGNOSIS OF CEREBRAL PALSY IN INFANCY

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Many workers in the field of cerebral palsy are agreed that an early diagnosis is of great importance and that better and quicker results can be expected from early treatment. Very early treatment, if possible before the age of 6 months, gives a child the best chance of improvement for the following reasons:

(1) In the infant, motor behaviour is largely reflex, and the higher centres of the central nervous system are only beginning to mature. During the first six to 12 months of the baby's life the use of the neural mechanism and its patterns can be influenced and directed more easily than later on. Gooddy and McKissock (1951) have stressed the importance of age for adjustment and learning in cases of brain lesions, and say:

> 'Whatever the underlying anatomical basis for residual function may be, we note that the facility with which the patient can readjust himself to cerebral damage seems to be related to his age on the one hand and to the rate of progress, if any, of the causal lesion on the other. The younger brain, like bodily tissues and organs, seems more adaptable and "plastic" than the older.'

(2) An infant with cerebral palsy does not usually show appreciable degrees of spasticity, and movements are not yet interfered with by the resistance of opposing hypertonic muscles. Movements can therefore be encouraged more easily at this stage, and early treatment, by facilitating normal movements, often prevents the development of spasticity (Bobath and Bobath, 1954, 1955).

(3) In untreated cases of cerebral palsy spasticity develops and increases in strength, its typical distribution resulting in the well known abnormal postures of the patient. If the patient maintains these abnormal postures for long, contractures and deformities are likely to occur. These are never seen in the infant and young child and can be prevented by early treatment.

(4) Cerebral palsy is a sensori-motor disorder. Movements are the response to sensory stimulation. They give the child a great variety of sensory experiences. To return to Gooddy and McKissock (1951):

> 'There is not a standard brain with all its functions set and localized for use. The brain stands ready for training. It learns, is trained, by appreciating input, sensation. It can then effect voluntarily what it has before done involuntarily.'

A child's intellectual development is dependent on both environmental stimulation and the appreciation of his own body as a result of proprioceptive stimulation. During the first year of a child's life his mental growth is dependent on an unimpeded development of his motor abilities. A child deprived of the ability to raise his head, to look around, to reach out for an object and bring it to his mouth, to acquire hand-eye coordination, and to sit up and move around to explore his environment, cannot but fail to advance in his mental development. If, in the severely handicapped child, the inability to move is not overcome at an early age, mental retardation will result and may in time become indistinguishable from mental deficiency.

Intelligence in Children with Cerebral Palsy

The correct or even approximate assessment of mental endowment of babies with cerebral palsy is extremely difficult and no satisfactory solution to this problem has so far been found. Collis (1953, 1954) has attempted to find tests for the detection of mental deficiency in infants with cerebral palsy as early as at 4 months of age. According to Collis, the unmodified reflex behaviour of an infant at that age has to be regarded as symptomatic of mental deficiency. To quote Collis (1954):

> 'Where the four month old child shows little or no diminution of the reflex quality of his activity and (apart from growth) little change in his appearance, mental deficiency can be presumed.'

All tests described by Mrs. Collis are tests of motor ability only, and are quite unsuitable for the detection of mental defect. The tests serve only to

separate the moderate from the severe cases of cerebral palsy, rejecting the latter from treatment on the grounds of mental deficiency. If accepted, they will exclude from early treatment just those severely affected children who are in most urgent need of it. As long as we have no reliable means of assessing intelligence at an early age it seems better to give every young child a chance of treatment. In the course of treatment it will often be seen whether a child can make proper use of his improving motor abilities and in this way we may come to a better understanding and more correct assessment of the child's potential mental ability. Even if the child should later on prove to be mentally defective, treatment may help him to become, physically at least, partly independent, and deformities may be prevented.

Definition of the Condition

As ideas about the nature of cerebral palsy differ widely, we shall first define our concept of the condition and discuss some points which form the basis of the tests upon which we rely for the early detection of cerebral palsy.

Cerebral palsy is not one condition but a group of conditions, the result of abnormal brain development or brain damage. We find in all cases an impaired motor function and an abnormal degree and distribution of muscle tone. This may be associated with speech defects (dysarthria or aphasia), hearing defects (of the conductive or perceptive type), visual defects (subnormal vision, field defects or ocular motor defects) and mental defect.

It is beyond the scope of this paper to go into the problems of incidence, aetiology and classification of cerebral palsy. These subjects have been discussed in great detail by Asher and Schonell (1950), Holoran (1952), Balf and Ingram (1955) and others. It is difficult enough to devise a satisfactory classification of cerebral palsy in older children. In the very young ones, under 12 months of age, in whom definite signs of cerebral palsy such as spasticity or involuntary athetoid movements are not yet seen, a correct classification is rarely possible. For instance, in a quadriplegic child one side of the body is usually more affected than the other. When very young, the child may only show definite abnormal signs on the more affected side, so that we may arrive at a diagnosis of hemiplegia. Some babies may show spasticity fairly early but may develop athetosis at about 18 months of age, while others may seem limp and ataxic and only develop pronounced spasticity later on. Other infants may show spasticity in the legs and no abnormal signs in the trunk and arms until later on when they try to sit up and use their hands; the initial diagnosis of spastic paraplegia may then have to be changed into one of diplegia.

The difficulty of classification at an early age is enhanced by the fact that many cases of cerebral palsy are of a mixed character. Whereas pure cases of spasticity are frequent among the hemiplegics and diplegics, quadriplegics often show athetosis, and most athetoids show various admixtures of spasticity or ataxia. In spite of these difficulties we should be able to make a diagnosis of cerebral palsy at an early age, though a differential diagnosis may be impossible.

We give below some figures which may be a pointer towards the relative significance of some aetiological factors. They are of 190 consecutive cases on our files of which we could obtain reliable birth histories by personal interview. Of these 190 cases, 33 showed normal birth histories and five had acquired cerebral palsy in early childhood. Of the remaining 152 cases, 36 were born prematurely. They, and the remaining 116 cases, showed the following birth histories:

Premature		Full-term Abnormal Labour	
Blue or white asphyxia, oxygen given (2 jaundiced)	17	36 (10 precipitate labour, 4 prolapsed cord, 1 jaundiced)	
Forceps delivery (breech presentation)	1	37 (7 asphyxiated, 2 prolapsed cord)	
Rhesus incompatibility (1 asphyxiated)	2	8	
Toxaemia of mother ..	1	9 (3 jaundiced)	
Neonatal jaundice	4	3	
Prolapsed cord	0	2	
Caesarian section	0	7 (2 asphyxiated)	
Precipitate labour	3	6	
Prolonged labour	3	8 (4 breech presentation)	
Premature only	5	0	
Totals ..	36	116	

It will be seen from the above figures that the factors at birth most responsible for cerebral palsy in this group of 152 cases were asphyxia, forceps delivery, prematurity and prolonged and precipitate labour.

The number and the percentage of cases in the present series attributable to these four conditions as well as the figures given by Asher and Schonell are shown in the accompanying table:

Causal Factor	No. of Cases	Present Series (152 Cases)	Asher and Schonell
Asphyxia	62	40%	38%
Forceps	38	25%	24%
Prematurity ..	36	24%	No comparable figures
Prolonged and precipitate labour	30	20%	15%

Some Relevant Points of Early Normal Motor Development

In the normal child motor development takes place in an orderly sequence (Gesell and Amatruda, 1947; McGraw, 1943; Thomas and Saint-Anne Dargassies, 1952). The normal baby shows a preponderantly flexor tone during the first two months of life. The limbs are held in flexion and resist passive extension. The distribution of flexor tone is strictly symmetrical. Even when kicking the baby does not extend his legs fully until he is about 6 months old. Under normal circumstances extensor tone develops gradually from the second month onwards, when the baby raises his head in prone lying and extends his spine against gravity, supporting himself first on his forearms and later on his extended arms. At about 6 months of age the baby lifts his buttocks off the support when lying on his back, supporting himself on his shoulders and feet, thus extending his spine and hips. In this way he prepares for the upright posture, for sitting, standing and walking. The influence of certain primitive reflexes, the tonic or static reflexes of Magnus (1926), can be seen in the normal baby. For instance, the asymmetrical tonic neck reflex shows itself in typical attitudes of the baby, face turned to one side and the 'face-arm' extended, the opposite arm flexed. One can observe this attitude more clearly and more frequently from the fifth week onwards, that is, at a time when extensor tone develops. The influence of the tonic reflexes diminishes after 4 months and then gradually disappears. Tonic reflexes, however, are never strong in the normal baby. They do not produce a stiffening of the baby's limbs and they do not interfere with his movements.

The Early Motor Development of Children with Cerebral Palsy

Like the normal baby, infants with cerebral palsy show at first a preponderance of flexor tone. It is only at the stage of developing extensor tone that the child with cerebral palsy becomes spastic. The speed and development of spasticity and its degree depend on the severity of the case. With the onset of spasticity we can observe an increase in the strength of the aforementioned tonic reflexes. Instead of disappearing, they gain in strength, and in time they may dominate the child's motor activities. They are coexistent with spasticity and prevent the further maturation of the child's motor behaviour. They are responsible for the typical distribution of spasticity throughout the body musculature. They produce changes of tone in predictable patterns when the position of the whole body in space is changed, or when the relation of the head to the body is changed.

In trying to make an early diagnosis, we search for signs of activity of tonic reflexes before they attain their full strength. Early diagnosis is easy in the severe cases in which spasticity and tonic reflexes develop quickly and strongly. In the milder cases they appear later, are more insidious and have to be provoked by special handling. In the athetoid patient they are less constant, and show themselves in the form of intermittent tonic spasms of variable strength. They have been observed by Ingram (1955) who calls them 'dystonic attacks'.

The tonic reflexes, which have been described in some detail in previous papers (Bobath and Bobath, 1954, 1955), include the tonic neck reflexes, the tonic labyrinthine reflexes and the positive supporting reaction. Only these, which are most important for diagnostic purposes, will be mentioned in this paper.

Asymmetrical Tonic Neck Reflex. This consists of an increase of extensor tone in the limbs to which the face is turned, and an increase of flexor tone in the limbs to which the skull is turned. The 'face-arm and leg' may extend, the 'skull-arm and leg' flex.

Tonic Labyrinthine Reflexes. These produce maximal flexor tone throughout the whole body in lying prone (face downwards), and maximal extensor tone in the supine position (face looking upwards).

Positive Supporting Reaction. This produces rigid extension of the leg, making it a 'pillar for weight-bearing' when the ball of the foot touches the ground.

As mentioned before, the increase of the strength of these reflexes goes together with the development of extensor spasticity. In some, usually in the spastic children, we can observe a slow and gradual increase of tone over a prolonged period of time. Only in the most severe cases is spasticity already present and strong at a very early age. These children, when lying on the back, show stiffly extended legs which resist passive flexion and abduction. They show retraction of head and neck and strong asymmetrical tonic neck reflexes. The hands are usually fisted, the arm flexed at the elbows and abducted at the shoulders. If the arms are passively moved forward at the shoulder, extended at the elbow, strong resistance will be encountered. However, the majority of infants do not show

definite signs of spasticity at a very early age. This is especially so with paraplegic children, or with diplegic children whose upper extremities are little affected. These children may appear quite normal until they try to sit up or crawl. A few children with very mild affection may show spasticity only when they attempt to stand or walk.

Athetoid children do not usually show involuntary movements before the twelfth or eighteenth month. of age and sometimes not before they are 2 years old These babies give the impression of being hypotonic. They may hardly move at all when they are very young, lying quietly on the back. When picked up they have no control over head and trunk; they are just floppy. The legs are usually flexed and widely abducted with an exaggerated dorsiflexion of the ankles. Some athetoid children wave their arms about aimlessly and seem to be unable to direct them in reaching out for an object. This initial state of limpness or flaccidity begins to alternate with transient phases of stiffening which becomes stronger and more frequent as the child develops, and when he tries to move and maintain his posture against gravity.

In order to arrive at an early diagnosis the task before the doctor is to differentiate between a general retardation of the child's motor development and early signs of spasticity or intermittent spasms. For this purpose we need special tests which provoke signs of spasticity while they are still latent. In other words, during examination the child is handled in a way which provokes abnormal spastic reactions.

Tests for Examination

A number of tests will be described, none of which alone is more than a pointer to a diagnosis. The certainty of the diagnosis is in direct proportion to the number of tests found positive.

Testing in the Supine Position. This is the position of maximal extensor spasticity due to tonic labyrinthine reflex activity.

TESTING FOR RETRACTION OF HEAD AND NECK. The examiner's hand is placed behind the child's head and an attempt is made to lift the child into the sitting position. One can feel the head and neck pressing backwards or, in the more severe cases, the whole spine may arch backwards. The arms, instead of moving forward on the chest as in the normal child, are retracted at the shoulders (Fig. 1). Head and neck retraction explain the child's inability to lift the head actively in the supine position, a preliminary to sitting up.

TESTING FOR RETRACTION OF THE SHOULDERS. The examiner grasps the arms of the child at the elbows and moves them forward and across the child's chest. Resistance to this movement can be felt and the arms pull backwards. This explains the child's inability to bring his arms forward and to pull himself up to the sitting position, especially as he is unable to lift his head.

TESTING FOR THE INFLUENCE OF THE ASYMMETRICAL TONIC REFLEX ON THE ARMS. As already described, the infant usually lies on his back with the arms in abduction and flexed at the elbows. The examiner turns the head of the child to one side and holds it in this position for a few seconds. The arm to which the face is turned may then extend spontaneously, while the contralateral arm becomes more flexed (Fig. 2). In some cases the 'face-arm' may not extend spontaneously, but passive extension of the elbow will be less resisted than before the face was turned

FIG. 1.—Extensor spasticity in the extensor position.

FIG. 2.—Asymmetrical tonic neck reflex.

towards that side, while passive extension of the 'skull-arm' will be more resisted. If asymmetrical tonic neck reflexes are present, it is difficult, or impossible, for the child to grasp an object with the hand to which his face is turned, while he can do so with the hand to which the skull is turned. This means that he cannot look at the object when grasping it. Asymmetrical tonic neck reflexes explain the child's inability to approximate both hands in the midline, his inability to bring his hands to his mouth and of acquiring hand-eye coordination.

TESTING FOR ABSENCE OF NECK RIGHTING REFLEX. On turning the head of an infant to one side, the body should follow the head and the child turn over to that side. This is a normal reaction up to 3 years of age. In severe cases of cerebral palsy the child will remain on his back and only an asymmetrical tonic neck reflex will occur. Such children are unable to turn over by themselves. In less severe cases the body may turn but the uppermost arm remains retracted. Such children may be able to turn over to their side, but only slowly and with difficulty.

TESTING FOR EXTENSOR SPASTICITY OF LEGS. The examiner grasps the legs of the child below the knees and moves them quickly upward to flex them against the abdomen. Resistance to this movement is noted. If the legs are suddenly released, they extend immediately and may adduct and even cross. If one leg only is flexed passively, the other leg may extend stiffly and rotate inward with plantiflexed foot (crossed extension reflex). In some children, however, both legs may flex when one is passively flexed. Resistance to passive flexion of the legs and the child's inability to keep them flexed after they are released, denotes extensor spasticity at the hips, and this explains the child's difficulties in sitting up and his tendency to fall backwards when sitting. A normal child rarely falls backward when he is yet unable to sit unsupported. It also explains the child's inability to kick in the normal way.

TESTING FOR ADDUCTOR SPASTICITY OF THE LEGS. Adductor spasticity is usually combined with extensor spasticity. It is, therefore, best tested with the legs in extension. The examiner grasps the legs below the knees and moves them quickly apart. Resistance to the movement is noted.

Tests in the Prone Position. This is the position of maximal flexor spasticity due to tonic labyrinthine reflex activity.

TESTING FOR ABSENCE OF PROTECTIVE SIDE-TURNING OF HEAD. A normal baby when lifted up and placed on his abdomen will turn the head to one side. This is a protective reflex, already present at birth. If flexor spasticity is marked a child with cerebral palsy will not do this but will remain face downwards on the support (Fig. 3). For this reason children with involvement of trunk and upper extremities cannot tolerate the prone position as they cannot keep the air passages free. We consider the inability to tolerate this position a valuable sign at a time when other symptoms may not yet be present.

TESTING FOR FLEXOR SPASTICITY OF ARMS. The child with cerebral palsy when lying on the abdomen shows flexion and adduction of the arms, the hands placed under the chest. The examiner grasps the hands of the child and moves the arms upwards so that they lie extended at the side of the head. Note is taken of the resistance to this movement. On releasing the arms they will return to their initial flexed and adducted position.

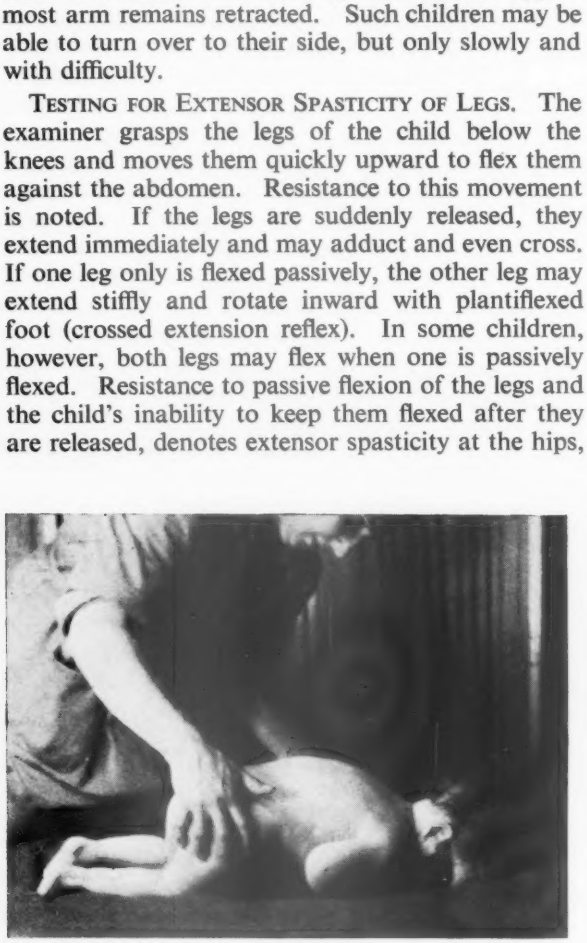

FIG. 3.—Absence of automatic turning of the head to the side in the prone position.

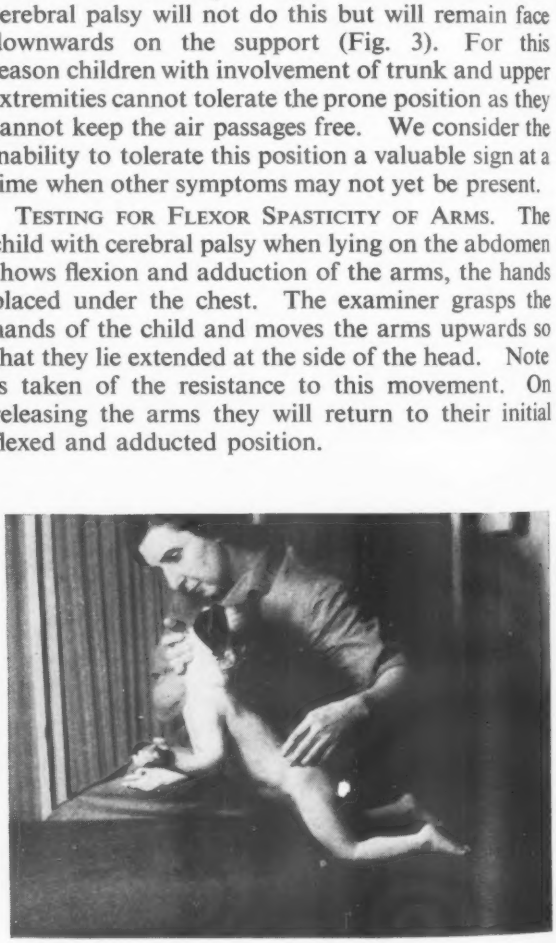

FIG. 4.—Absence of extension of the arms to support the weight of the body.

Another test is that of raising the child's head passively with the examiner's hand under the child's chin. In some cases resistance to this movement will be felt, that is, pressure downwards of the head against the examiner's hand. The normal reaction of a child of 4 months and onwards to raising the head is a protective extension of the arms, the hands being placed on the support. The child with cerebral palsy will draw up the arms in flexion and be unable to support his body weight on his hands. The hips may flex simultaneously (Fig. 4).

TESTING FOR EXTENSOR SPASTICITY OF LEGS. As mentioned before, flexor spasticity is maximal in the prone position, and in severe cases extension of the hips may be impossible so that the child cannot be placed on his abdomen. However, if the hips can be extended, this extension produces extensor spasticity at the knees and feet, though the trunk, neck and arms remain flexed. The examiner lifts the child's hips off the support, holding the pelvis around the iliac crests. If extensor spasticity is marked, the legs extend stiffly and it may be difficult to flex them passively. In less severe cases, the legs may flex spontaneously but only slowly and after considerable delay (Fig. 5).

One can also test for extensor spasticity by flexing the knees while holding the pelvis down to the support. This must be done with the thighs adducted, extensor spasticity being stronger with adducted legs. Resistance to passive flexion of the knees is then encountered. If the hips are released the knees may show less resistance to passive flexion, but the hips will flex as well (Fig. 6).

Flexor spasticity of the trunk and arms and extensor spasticity of the legs prevent the child from raising the head, and from getting on to his hands and knees to crawl.

Tests in the Upright Posture. The last tests are in the upright posture.

TESTING FOR EXTENSOR SPASTICITY OF THE LEGS. The examiner holds the child under the axillae in the air and lowers him slowly towards the support. The legs may then extend and the feet point downwards. In some cases the legs may adduct and even cross. On touching the support the child may support his body-weight and stand on his toes, with the legs rigidly extended. Some children with moderate spasticity may show reflex stepping, but cross the legs when doing so (Fig. 7).

Other children, usually those who seem flaccid and lie supine with abducted legs, may draw up the legs in flexion when held up in the air. They will not support their weight on their legs when their feet touch the support. The examiner then 'bounces' the child several times in quick succession on his feet. An increase of extensor tone in the legs may then be noted, which may become stronger with each 'bounce' and result in a temporary stiffening of the legs. These children usually develop extensor spasticity in the legs later on.

The 'Landau' Reflex. The examiner holds the child free in the air supported under the abdomen. A normal child, from the age of 6 to 8 months onwards, will lift the head and extend his spine and legs (this reaction has disappeared by the age of 3 years). If the examiner flexes the head passively the whole body will flex. The 'Landau' reflex is usually absent in the child with cerebral palsy. When held in the air, the child will neither raise his head nor extend his spine and hips. The knees, however, may be extended if extensor spasticity is marked. The absence of the 'Landau' reflex is due to the inhibiting influence of flexor spasticity on the

FIG. 5.—Resistance of the legs to passive flexion.

FIG. 6.—Flexion of the knees produces flexion of the hips.

FIG. 7.—When the child is held free in the air, the feet point downwards and the legs sometimes cross.

FIG. 8.—Absence of protective extension of the arms.

head and trunk when the head is facing downwards (tonic labyrinthine reflex).

Protective Extension of the Arms. This reaction, as well as the one above, has been described by Schaltenbrand (1927). The latter was called '*Sprungbereitschaft*'. As in testing for the 'Landau' reflex, the examiner lifts the child up, holding him around the waist, and then lowers him slowly downwards towards the support. A normal child from 4 to 6 months of age onwards will extend his arms and hands to reach out for the support. A child with cerebral palsy will draw up his arms in flexion (Fig. 8). In less severe cases the arms may extend protectively when the head touches the support.

Summary

A number of tests have been described to assist in the early recognition of cerebral palsy. They are based on the work of Magnus (1926) and Schaltenbrand (1927), and demonstrate the presence of abnormal postural reflex activity. The diagnosis is based on the interpretation of the child's motor disabilities in terms of abnormal postural reflex activity.

We wish to thank Dr. E. Ellis, Medical Director of the Percy Hedley School for Spastic Children, for his advice and valuable criticism in the preparation of this paper.

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THE SIGNIFICANCE OF THE SO-CALLED "IRRITABLE HIPS" IN CHILDREN

BY

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In spite of the extensive use of radiographs and laboratory investigations, it is still impossible to clarify the nature of the syndrome known as 'irritable hip'. Although the nomenclature of the condition varies, the term 'irritable hip' will be used in this paper because it does not prejudge either the aetiology or pathology and it has the added historical merit of having been used by Hugh Owen Thomas.

The syndrome is important not so much in itself but because of the difficulty in differentiating it from more serious conditions of the hip joint. Few articles have been written on this subject; I have found only 12.

Bradford (1912) called the condition a synovitis of the hip, saying that its diagnosis can be given only after the symptoms have subsided and no other cause of the condition has been found.

Todd (1925) described it as a simple transient coxitis and he recommended that the patient should be put to bed without any fixation for observation and differentiation from tuberculosis. Fairbank (1926) described eight groups of non-tuberculous coxitis in children and adolescents. Platt commented on Fairbank's grouping and also used the term 'observation hips'. This term is quite adequate because the patient must be kept under observation.

Miller (1931) described this syndrome and reported 77 cases of what he termed 'acute transient epiphysitis of the hip joint in children'. He said that some radiographs showed small abscesses and bone absorption near the epiphyseal line; 80% of his cases were associated with diseased tonsils. He believed that the radiological findings were due to embolic abscesses. His treatment was to remove the primary focus, with rest from weight bearing, and fixation of the hip by traction and the symptoms usually cleared up in a few weeks or a few months.

Butler (1933) investigated 97 cases of arthritis of the hip joint in children. Radiographs of 34 showed no abnormality and there was a complete return of function. They could therefore be classified under this syndrome, although Butler referred to them as transitory arthritis of the hip joint and believed that they were sometimes traumatic but more often infective. He also believed in the existence of an infection secondary to a focus elsewhere in the body.

Finder (1936) reported 22 cases of what he termed transitory synovitis of the hip joint. Rauch (1940) reported 37 cases of transitory synovitis of the hip joint in children and also suggested that the condition was due to an allergy. Wiles (1951) said that four out of five children and adolescents with symptoms in the hip joint had transient symptoms only.

Edwards (1952) reported 13 cases which he also called transient synovitis of the hip joint and he concluded that the condition represented an allergic hypersensitivity or toxic reaction to a focus of infection elsewhere in the body. Two of his patients responded dramatically to antihistamine therapy.

Drey (1953) found definite radiological changes with this syndrome. He described unilateral exaggerated shadows of the obturator internus, the iliopsoas and the gluteus minimus muscles, and believed that the swelling of these muscles was evidence of synovitis of the hip joint.

Hermel and Sklaroff (1954) reported two cases in which, in addition to the radiological changes described by Drey, the shadow of the distended hip joint capsule of the affected hip joint could be seen laterally.

Material

At the Orthopaedic Department of the City General Hospital, Sheffield, 46 children were treated in whom no pathology of the hip joint was discovered, even after prolonged observation and repeated examination.

Sex Incidence. Of the 46 patients, 37 (80·5%) were males and nine (19·5%) females. This incidence is similar to that reported by Butler (1933), where the boys predominated over girls in the ratio of 17:5. Edwards

(1952) reported that boys and girls appeared to be equally affected.

Age Group. The average age of the 46 patients was 7 years, the youngest being 2 years and the oldest 14 years. The average age group of Finder (1936) was 5·4 years.

Seasonal Distribution. In 20% of the 46 cases the onset was in May. The highest frequency noted was during the period April to August.

Preceding Factors. Three of the patients had been in contact with tuberculous members of their families. The brother of one patient was being treated for Perthe's disease. Four of the patients had recently been ill with tonsillitis, one with bronchitis and asthma and two with scarlet fever. One patient had had pyrexia for a few days, another attended while suffering from glandular fever, and seven had been reported as having sustained an injury.

The Syndrome

The predominant complaints are of pain and of a limp. The pain at the onset is not sufficient to cause alarm or to suggest a serious disease. Occasionally the pain radiates to the front of the knee. Few patients were unable to walk. In some the limp was very slight.

Of the 46 patients, 11 (24%) complained of pain only and 35 (76%) complained of both pain and a limp.

The onset of the symptoms in 25 patients (54%) was insidious and in the rest, 21 patients (46%), it was sudden. This corresponds with the findings of Edwards (1952) who reported the insidious and sudden onsets as being equal.

The right hip was involved in 24 children, the left in 22.

The average interval from onset to attendance for 41 patients was 17 days. The other five patients attended after a long interval and, if they had been included in addition to the 41, the average of all 46 would have been 77 days.

Clinical Findings. Sixteen of the patients (34%) were in-patients, while 30 (66%) were out-patients.

Twenty-seven (59%) had pain around the hip on active movement and 11 patients (24%) had some pain even when still. In all patients, however, the pain was slight and only one patient complained of the pain disturbing him at night.

Forty-three (93·5%) patients had pain on weight-bearing; three (6·5%) were free from pain on weight-bearing. The pain was described as slight in 93% and severe in 7%.

A limp was present in 43 (93·5%) patients.

Only five (11%) patients had any tenderness over the hip joint. No swelling was found in any patient. Twenty (43%) patients had a flexion deformity varying from 10° to 40°. There was limitation of extension of the hip joint in 15 patients (33%). Forty-three (93·5%) patients had limitation of internal rotation, but in only eight (17·5%) patients was the limitation virtually complete. Abduction was found to be slightly limited in 22 (48%) patients, moderately limited in 12 (26%) and full in 12 (26%). External rotation was full in 23 (50%), slightly limited in 18 (39%), moderately limited in three (7%) and severely restricted in two (4%). Forty-three of the children (93·5%) had muscle spasm, and in eight of these it was severe.

Four patients had a rise in temperature, which reached 100° in one patient and 99° in the other three. Finder (1936), Edwards (1952) and Hermel and Sklaroff (1954) all described a pyrexia to 103°, but this was not seen in the present series.

The Trendelenburg test was negative in all patients.

Laboratory Data. The white blood count was normal, ranging between 4,700 and 9,600. The differential count was also normal except that one child was also suffering from glandular fever with the typical changes, and the other had an eosinophilia of 12% due to intestinal worms.

The erythrocyte sedimentation rate ranged between 3 and 12 mm. in one hour. In one patient the E.S.R. rose to 27 mm., but when he was admitted to hospital he also had an infective dermatitis of the scrotum.

In only one patient was the Mantoux test positive and the mother of this child was suffering from active pulmonary tuberculosis.

There were no positive Wassermann and Kahn reactions.

In two cases the hip joint was aspirated, and culture and guinea-pig inoculation were negative for tuberculosis.

No patients had a biopsy of the synovial membrane performed as it was thought to be risky and unjustifiable in a condition which clears up without complications.

Radiological Findings. Although two authors have claimed typical radiological changes, none were found in this series. Two patients had a slight degree of bilateral coxa valga and one had osteo-

FIG. 1.—Radiograph, taken three days after the onset of symptoms, showing the oedema of the muscles in the neighbourhood of the affected hip joint.

poikylosis. In another there was a secondary centre of ossification in the inferior iliac spine. It was considered that none of these findings had any connexion with the symptoms.

Hefke and Turner (1942) reported the shadow of the obturator internus as an early diagnostic finding in septic arthritis and tuberculosis of the hip which was never present in any other condition.

The reported radiological findings of soft tissue shadows have been seen in cases of septic arthritis and osteomyelitis and tuberculosis. These shadows of distended capsule, and of swollen muscles with the translucent lines in the intermuscular septa showing, were not seen in the present series but

FIG. 2.—Antero-posterior view of the hip joints, taken eight weeks after the onset of symptoms, showing the subperiosteal new bone on the outer aspect of the left ilium.

FIG. 3.—Lateral view of the hip joints, taken eight weeks after the onset of symptoms, with the same subperiosteal new bone.

only in patients with an infective arthritis. For instance, in a 5-year-old girl with a three-day history of pyrexia and severe pain in and immobilization of the left hip, a radiograph showed oedema of the muscles in the neighbourhood of the left hip joint. It was considered that she had an infection near the joint and she was treated with penicillin. The pyrexia subsided after three days and all clinical signs had disappeared after four weeks, when fixation was removed. Radiographs taken eight weeks after the onset of symptoms showed subperiosteal new bone on the outer aspect of the left ilium just above the acetabulum indicating an osteomyelitis of the ilium. Three months later all the radiological changes had subsided.

Differential Diagnosis. The sole importance of the syndrome of irritable hip lies in the necessity to distinguish it from infective arthritis, tuberculosis, Perthe's disease, rheumatism, osteomyelitis, slipped upper femoral epiphysis and other less frequent

FIG. 4.—Radiograph taken three months later showing that the soft tissue and bony changes have subsided.

conditions. The differential diagnosis is easy eventually because, while an irritable hip settles down slowly without producing any specific sign, the other conditions always produce the typical signs both clinically and radiologically.

Treatment and Results

The treatment consisted of complete rest in bed with fixation by traction. The symptoms usually subsided with two to three weeks of non-weight-bearing exercises in bed. Practically all the patients had completely recovered within four weeks, six had some recurrence of pain in the hip joint and in these the total duration of symptoms averaged 37 weeks as opposed to the average duration in the remaining 40 patients of 4·2 weeks. In all the patients there was a complete remission of symptoms.

Two cases, not included in the series of 46 patients, are interesting as showing the importance of following up an apparent irritable hip. In one case, a boy aged 5 years, positive radiological changes of Perthe's disease did not show till 18 months after the start of a limp. In the other, a girl of 13 years, despite three admissions to hospital for investigation and treatment, abnormal radiographical changes were not observed until after 26 months and it was almost five years before a diagnosis of tuberculosis of the hip was confirmed. Early disappearance of abnormal physical signs and symptoms with fixation in bed does not rule out the possibility of latent serious disease.

In considering the follow-up, it must be realized that after a few weeks of fixation the symptoms subsided. It is, therefore, very difficult to persuade the parents to bring to the Out-patient Department what they consider to be a normal child. It is for this reason that the average attendance interval for each patient was 6·8 months and varied from one month to three years. During March, 1956, an attempt was made to re-examine all 46 patients but only 30 of them attended. The longest interval from the onset of symptoms to March, 1956, was eight years and the shortest six months. Each patient was found to be leading a normal life and clinical, radiological and laboratory examinations revealed no abnormal pathology in the hip.

Conclusion

The purpose of this paper is to draw attention to the condition of 'irritable hip'. It is a common condition in children but its incidence has been ignored because it is not a disabling condition. The aetiology of the syndrome is difficult to determine. It would be quite wrong in a briefly self-limiting condition to subject the patient to the risk of an exploration and biopsy. It is frequently forgotten that the joint lining consists of highly undifferentiated tissue and that therefore its power to respond differently to different stimuli is nil. The histological picture is essentially the same whether the irritation is due to infection, trauma, rheumatoid arthritis, osteo-arthritis or any other condition. It is quite wrong, for example, to report that 'the synovial membrane shows the typical histological changes of rheumatoid arthritis'. Even if tubercles are found in a joint, these are the specific reaction of any part of the body to tuberculosis, and the synovial membrane itself differs in no way from that produced by any other noxious stimulus. It is probably true to say, therefore, that there is no definite single aetiology in this condition.

Summary

The literature on the subject of 'irritable hip' has been briefly reviewed and 46 children with transient symptoms in the hip joint have been studied in detail. Irritable hip appears to be a definite clinical entity whose main importance lies in the necessity for careful observation and follow-up even for years after the symptoms have subsided.

I would like to thank Mr. S. Pappworth for permission to study his cases and for advice in the preparation of this paper, and Dr. C. N. Eccles for his valuable statistical assistance.

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SCLEREMA NEONATORUM: RECOVERY WITH CORTISONE

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Almost every paper about sclerema refers to the confusion surrounding the subject. This has arisen because the term has unfortunately been used to describe two very different conditions; the salient features of each are set out in the Table.

Thus the confusion is terminological rather than clinical. In reading the literature there is seldom any difficulty in classifying a case by its description as one or other condition, and the same has been my experience in half a dozen cases seen in clinical practice. Occasionally intermediate cases have presented difficulty and some atypical examples, such as the case described by Nicholson and Claireaux (1948) which appeared to be a form of generalized infective cellulitis in an older baby, defy classification. A third condition, characterized by localized pitting oedema in cold premature babies, is sometimes called scleroedema but this is not always easy to differentiate from fat necrosis. Scleroderma with sclerodactyly is a disease of the skin which probably does not occur in infancy.

The generalized disorder in young babies (to which the term sclerema neonatorum will be confined here) was first recorded by Usenbenzius (1722) who described a newborn baby that was intensely cold and rigid. Underwood mentioned the condition in his book in 1784, but described it in full in a later edition (1819) under the heading 'skin bound'. He acknowledged assistance from Dr. Denman in making the following list of pathognomonic symptoms:

> '1st. The skin is always of a yellowish-white colour, giving the idea of soft wax.
> 2d. The feel of the skin and flesh is hard and resisting, but not oedematose.
> 3d. The cellular membrane is fixed in such a manner that the skin will not slide over the subjacent muscles; not even on the back of the hands, where it is usually very loose and pliable.
> 4th. This stricture often extends over the whole body; but the skin is peculiarly rigid in the parts about the face, and on the extremities.
> 5th. The child is always cold.
> 6th. The infant makes a peculiar moaning noise, which is often very feeble; and never cries like other children.
> 7th. Whatever number of days such children may survive, they always have the appearance of being dying.'

TABLE

FEATURES OF TWO FORMS OF SCLEREMA

	Acute sclerema Pre-agonal induration Cadaveric induration	Pseudo-sclerema Subcutaneous fat necrosis Subcutaneous fat sclerosis
Synonyms		
Onset	Usually first week of life Occasionally later associated with diarrhoea and dehydration	First week of life
Distribution	Generalized (most marked in the legs; palms, soles and genitalia often spared)	Localized (circumscribed areas often symmetrically placed on the back, buttocks or shoulders)
Description	Normal appearing skin tightly bound down to underlying tissues restricting mobility of chest and joints	Discoloured skin overlying swollen plaque with irregular but definite margin; not deeply attached to underlying structures
Temperature control	Poor	Normal
Aetiology	Unknown	Birth trauma, ? infection, ? cold
Prognosis	Bad	Good
Histology	Normal, or slight increase in subcutaneous connective tissue	Gross destruction of normal picture with neutral fat crystals, giant cells, coarse trabeculation and sometimes calcification and cyst formation

Hughes and Hammond (1948), in an excellent review of the subject, collected 16 definite cases from the literature and added three of their own. In 16 the disease began in the first week of life and in this type of case the picture is less likely to be complicated by infections. Only five of the 19 cases survived. Unfortunately their attempt to clarify the nomenclature has not always been heeded. Brain (1953), in a clinical description of a case of fat necrosis under the heading 'sclerema neonatorum', perpetuates the confusion by stating:

> 'Pre-agonic or cadaveric induration is so obviously an ante-mortem solidification of the fat in a marasmic, moribund infant that it could scarcely be confused with sclerema neonatorum, except in the rare case when the latter disease involves the trunk and limbs, with in consequence, a serious prognosis.'

His predilection for the term 'pre-agonic induration' can hardly be justified now that the disorder has been shown to respond so well to treatment.

Case Report

After a normal pregnancy Mrs. N. gave birth without difficulty to her first baby with the assistance of a midwife at her home. The infant, a boy weighing about 6½ lb., was noticed to have rather stiff legs from the first. He was unable to suck from the breast but expressed breast milk was given with some success from a spoon. His stiffness, immobility and difficulty with feeding increased so that on the fifth day the family doctor (Dr. Kay) was called in. At his request the baby was seen by me on the following morning and immediately admitted with his mother to hospital.

On examination he was a thin, wizened, immobile baby with a weak, hoarse cry and with a subnormal temperature too low to record. He weighed only 5 lb. 2 oz. The skin over the whole body was bound tightly down to the subjacent tissues and could not be picked up from them. The knees and hips were flexed and could not be extended. The cheeks and lips felt woody and the chest expanded poorly. Fine crepitations were audible over both lung fields and the air entry was diminished. In short, the baby seemed certain to die but it was felt that nothing would be lost by the experimental administration of cortisone.

Therapy was started at once (aged 6 days) with cortisone 25 mg. t.d.s. and tetracycline 50 mg. b.d. given by tube. The baby was nursed in an oxygen box and fed with expressed breast milk by tube. Within a few hours of the first dose he seemed a little looser and thereafter steady improvement took place without interruption. The temperature (97° F.) was first recordable on the second day and became normal on the third. The face softened on the second day and the baby was able to suck from the breast for the first time though tube feeding was continued until the third day after admission. The arms and chest became normal by about the fourth day but slight woodiness of the tissues of the thighs and calves persisted for about one week. Cortisone was reduced from 75 mg. to 50 mg. daily on the sixth day and subsequently the dose was gradually reduced until it was discontinued on the tenth. In all the baby received 570 mg. The daily dose of tetracycline was reduced concurrently and was discontinued at the same time. He was discharged on the twelfth day weighing 6 lb. 3 oz. partly breast fed. Full recovery had apparently taken place and no relapse occurred.

Discussion

At the time when this baby was seen the writer was unaware of the good reports of cortisone and corticotrophin therapy that had appeared in the American journals. The first was by Kendig and Toone (1951) who described a typical case in a premature baby. Treatment with oxygen and penicillin began on the third day but the condition worsened. Cortisone, 10 mg. t.d.s., was begun on the fourth day by mouth; a total of 80 mg. was given over a five-day period. Recovery evidently took place in 36 hours. A very similar case with the same dramatic outcome was reported by Kendall and Ledis (1952) who gave A.C.T.H., 5 mg. six-hourly, by injection. Williams (1953), also unaware of the previous reports, described a case successfully treated with A.C.T.H. but the subsequent progress was marred by superadded infections and the development of bilateral cataracts. Eisenoff, Aaron and Green (1954) reported two successful cases, one similar to those cited above in which the disease began in the first week of life and the other in which a 6-week-old baby developed diarrhoea, dehydration and generalized sclerema four days later. Likewise Buess (1955) reported three recoveries, one being a typical neonatal case and the other two were older infants suffering primarily from diarrhoea and dehydration. In the latter type it is difficult to assess the relative importance of fluids, antibiotics and corticotrophin in aiding recovery. Davis (1955) mentions four recoveries with cortisone or A.C.T.H. but gives details in only one, a newborn baby given intramuscular cortisone, 25 mg. daily.

There are no reports of failure of these hormones in this condition but there are descriptions of two cases in which the response to therapy was not dramatic in the way that is characteristic of the other recoveries. Søndergaard and Nielsen (1954) reported an atypical case of a baby aged 31 days whose indurated areas improved with A.C.T.H. (nine day course, total dosage 80 mg.) but which failed to disappear entirely after a second course (13 days, total dosage 130 mg.) and were still detectable seven months later though they finally resolved but the child was mentally defective. The other case

(Fauser, 1954) is stated to have been unaffected by A.C.T.H. but to have responded dramatically to cortisone; however, from the description fat necrosis seems to have been the condition and perhaps spontaneous recovery is the true explanation of the conflicting therapeutic results.

In sum, therefore, including the present report, since 1950 there have been seven dramatic recoveries in uncomplicated cases of generalized sclerema which was present at or developed a few days after birth, three recoveries in older babies suffering also from severe diarrhoea, five cases which, for various reasons, are difficult to assess and classify, and no failures.

It seems very probable that cortisone and corticotrophin have been mainly responsible for this excellent recovery rate in a hitherto very dangerous condition. Admittedly nearly all the cases also received antibiotics which no doubt played their part but nevertheless the improvement seemed to coincide with the hormonal therapy. Furthermore, in the period when these hormones have been available but not given deaths have still been recorded (Grotts, 1951; Rodriguez Fuentes, 1955). As already stated, Hughes and Hammond collected four reports of recoveries and added one of their own but in none could the response be described as dramatic with the possible exception of one treated by hot baths (Allyn and Marek, 1933) which recovered in ten days whereas in others the disease was protracted to several weeks. Other treatments claimed to have been successful include thyroid administration (Bourne, 1922) and blood transfusions (Lund, 1950).

The dosage of A.C.T.H. has been fairly uniform and this has been the most usual form of therapy. Cortisone has been given by injection in one case and by mouth in two. Kendig and Toone gave only 80 mg. in all to a baby weighing 3 lb. 12 oz. whereas the total dosage in my case (weight 5 lb. 2 oz.) was 570 mg. No doubt this was unnecessarily large but the situation was desperate and no harmful effects were observed.

Summary

A case of generalized sclerema neonatorum is described which responded dramatically to oral cortisone.

In recent years there have been six other similar case reports of rapid recovery with A.C.T.H. or cortisone.

No failures with this form of therapy have been reported.

The term 'pre-agonal induration' is no longer appropriate.

My thanks are due to Sisters Hume and Holdsworth and to the ward nurses for their skilful care of the baby.

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DUPLICATION OF THE STOMACH

BY

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Duplications of the alimentary tract, and of the stomach in particular, are seen very rarely and for this reason alone they may escape diagnosis. It is, therefore, considered instructive to describe a case of gastric duplication treated successfully by resection.

Case Report

A female infant aged 4 weeks was admitted to the City Hospital, Aberdeen, on March 31, 1955. Ten days previously she had an episode of vomiting, and on the day of admission she passed a green, slimy stool. At birth she weighed 9 lb. 4 oz. and delivery was spontaneous at full term. She was fed on breast milk for two weeks after birth but the supply became insufficient. Before admission she was receiving 5 oz. of a mixture of cow's milk and water four-hourly five times daily.

Her brother, aged 5, and her mother were well, but the father was in hospital with acute nephritis.

On examination the baby was small but not dehydrated. Her weight (8 lb. 10 oz.) indicated retarded growth. A smooth swelling, 1×2 in. in area, was visible in the left hypochondrium; it was firm and apparently fixed but it could be partially surrounded by one's fingers. When the baby was fed, however, the swelling became firmer and moved downwards and inwards. No peristalsis was seen. A mouthful of feed was possetted but no true vomiting occurred.

Four days after admission a barium meal was given but there were no diagnostic radiological findings. The abdominal mass remained unchanged. However, the baby fed well and gained weight until April 12 when she developed symptoms of gastro-enteritis due to cross-infection with *E. coli* O111B4. On one occasion during this illness frank blood was observed in the stool. Despite antibiotic (tetracycline) therapy cultures of stool remained positive. The baby gradually regained her health, however, her appetite returned and she gained in weight, but the abdominal swelling remained unchanged.

On July 1 radiological examination was repeated. No abnormality was detected after a barium meal until the baby sucked from an empty bottle and thus distended the stomach with air. The tumour was then seen protruding into the stomach and appeared to be attached to the middle part of the greater curvature (Fig. 1). Laparotomy was advised and the baby was therefore transferred to the Royal Hospital for Sick Children, Aberdeen, for surgical treatment.

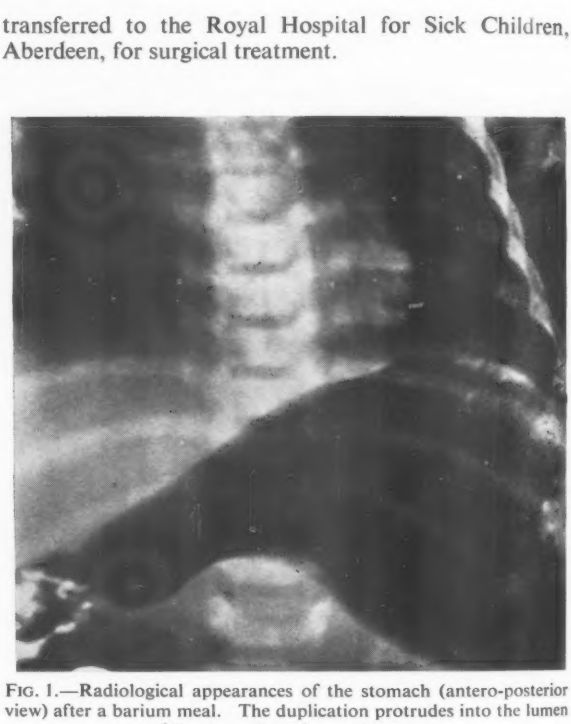

FIG. 1.—Radiological appearances of the stomach (antero-posterior view) after a barium meal. The duplication protrudes into the lumen of the stomach at the greater curve.

Operation. Under general anaesthesia (gas, oxygen, ether) Mr. S. G. Davidson performed, a laparotomy through a right paramedian incision. A smooth, oval cystic mass, approximately $2 \times 1 \times 1$ in., was attached midway along the greater curve of the stomach and was also bound by fibrous adhesions to the transverse colon and pancreas. Much of the wall appeared to blend with that of the stomach, while at one point it was firmly adherent to the colon, the appearances suggesting a small, partially-healed inflammatory and ulcerated focus. After dissection from the colon, the mass was removed together with a fringe of stomach wall, $\frac{1}{2}$ in. wide, and a small piece of pancreas. No communication was observed between the cavity of the cystic lesion and the stomach lumen. After the resection the stomach wall was sutured and an aspiration tube manipulated into the duodenum.

Pathological Findings. The specimen consisted of a cystic structure shaped like a kettledrum (Fig. 2) and measuring 5×3×3 cm. It had a thick muscular wall which merged into the muscle layer of the attached oval-shaped portion of true stomach and it was covered exteriorly by peritoneum. At one point on its lower convex border there was a small granulomatous nodule surrounding a minute orifice. Some 2 ml. of slightly mucinous but otherwise watery fluid was 'milked' through this hole by compression. The fluid had a *p*H of 4·0 and contained pepsin but no free hydrochloric acid. When the specimen was bisected a cavity was seen, approximately 3 cm. in diameter lined by pink, healthy-looking mucous membrane partially folded into small rugae (Fig. 3). There was no communication between the cavity and the overlying stomach.

Microscopic examination of the cystic structure showed that its mucous lining was like that of normal gastric mucosa (Fig. 4), with chief and parietal cells easily identifiable. There were no active erosions or ulcers, but the appearances of the mucosa around the small orifice on the distal border, where there had been adhesion to the transverse colon, were suggestive of healed erosion. There was a well-defined muscularis mucosae beneath the mucous membrane and external to this were a submucous layer of connective tissue and then a thick muscle coat, most of which was covered by peritoneum. In many parts of the cavity wall two muscle coats, an inner circular and an outer longitudinal, were distinguishable; these blended with the muscle coat of the true stomach, thus accounting for the surgical impossibility of removing the cyst by dissection. Auerbach's and Meissner's nerve plexuses appeared to be normal.

The appearances thus conformed to those of so-called 'duplication of stomach'.

Progress. The condition of the baby after operation was uneventful except for some reluctance to take feeds. She was discharged home August 4, when she weighed 11 lb. 12 oz. On January 4, 1956, there was still a little difficulty in feeding but the weight was 17 lb. 4 oz. A further radiological examination revealed no abnormality of the vertebrae, particularly in the cervical and upper dorsal region, but an opacity was seen in the right lung field at the level of the hilum (Fig. 5). It did not pulsate and it caused no oesophageal displacement. Moreover, no calcification was seen in it. The significance of this abnormality is uncertain but it may be a mediastinal cyst of foregut origin. No surgical interference is at present contemplated, but the infant is being kept under close observation.

Discussion

The baby was admitted to hospital because of green, slimy stools and failure to thrive, not because of an abdominal tumour. When the latter was observed clinically it was thought to be either a double stomach or a cyst. The correct diagnosis of duplication of stomach was suggested by radiological examination after a barium meal when the abnormality was seen to be outside the stomach but could yet be invaginated into it.

Duplications are ' spherical or elongated hollow structures which possess a coat of smooth muscle, which are lined by a mucous membrane, and which are intimately attached to some portion of the alimentary tube' (Ladd and Gross, 1941). They are more common in relation to small intestine than to any other part of the alimentary tract, and they are usually observed in childhood but may be found at any age. The lining is alimentary in type but does not necessarily correspond to that at the level at which the duplication is found, e.g., a rectal cyst may have a partial lining of gastric mucosa. In some specimens there are two or even three types of alimentary mucosa. In Ladd and Gross's series of 18 cases of duplication the sites were: base of tongue, in one patient; oesophagus, in three; stomach, in one; duodenum, in one; jejunum, in two; ileum, in seven; caecum, in one; sigmoid, in one; rectum, in one. Their case involving the stomach was in a 6-year-old girl; the lesion was on the greater curve and posterior surface and was almost as large as the stomach.

Duplications may or may not communicate with the lumen of the adjacent hollow viscus. In the case under discussion there appeared to have been ulceration from the duplication into the transverse colon; this, we presume, was a possible cause of melaena.

Signs and symptoms of duplication arise most commonly from mechanical obstruction to part of the normal alimentary tube. Repeated haemorrhage, associated with peptic ulceration, has also been described. The radiological findings are very helpful in diagnosis, while at laparotomy the intimate union of the muscle coat of the duplication with that of the adjacent alimentary tract is important in the recognition of the condition. Mesenteric cysts which may be confused with abdominal duplications can usually be dissected free and are, moreover, thin-walled. In our patient the movement of the abdominal swelling, observed clinically, is attributable to the firm attachment of the duplication to the greater curve of stomach: as the stomach became distended with food, the swelling moved downwards and inwards towards the midline.

Several theories have been advanced to explain the formation of duplications. The most popular is the 'sequestration theory', viz., groups of cells from the primordial intestinal tube become pinched off. In this connexion it is of interest that Lewis and Thyng (1907) frequently found diverticula in various portions of foetal alimentary tract in pigs.

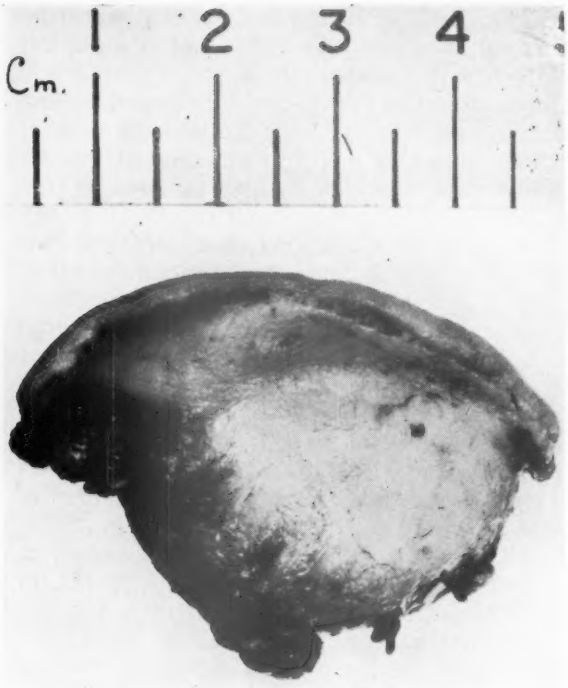

FIG. 2.—Lateral view of the resected specimen. The upper part is covered by a part of the normal stomach wall.

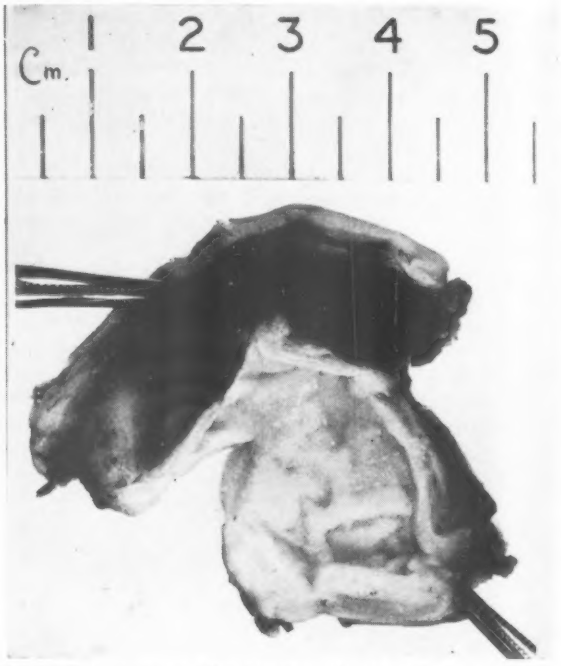

FIG. 3.—The specimen after bisection showing its rugous mucous lining.

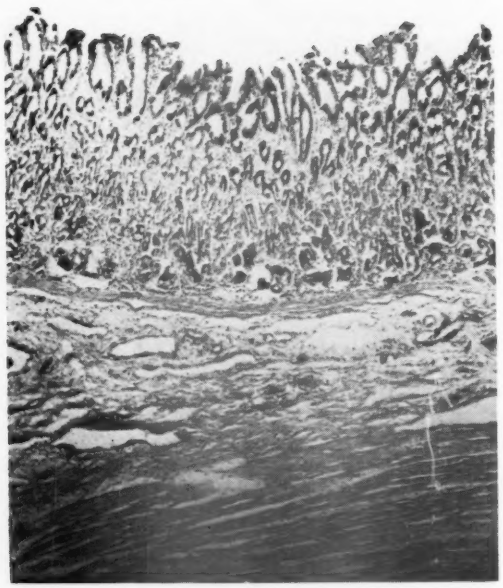

FIG. 4.—Section of the wall of the duplication showing a mucous membrane like that of normal body of stomach. Haematoxylin and eosin, ×40.

FIG. 5.—Radiological appearances of the thorax (antero-posterior view) showing the mediastinal opacity.

rabbits, cats, sheep and man. These were seen most often in the ileum but were unrelated to a Meckel's diverticulum and usually regressed.

We have mentioned the radiological finding of an opacity in the chest and have suggested the possibility of it being due to a mediastinal cyst of foregut origin. Fallon, Gordon and Lendrum (1954) have given an excellent account of such cysts which are commonly associated with vertebral anomalies and sometimes with mesenteric cysts and duplications. They emphasize that the association of such mediastinal cysts with anterior spina bifida has not been adequately appreciated and they regard such cysts as the final result of an abnormal extension of the lumen of the foregut produced on its posterior aspect by incomplete separation of the notochord. Consequent interference with anterior fusion of the vertebrae brings about the vertebral anomalies. Later in embryonic development the cyst tends to move caudally by growth of the intrathoracic viscera.

Summary

A case of duplication of the stomach is described and points of diagnostic value are indicated.

We are indebted to Mr. S. G. Davidson, Dr. A. M. Stewart and Professor J. S. Young for their help and advice.

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BOOK REVIEWS

Biologische Daten für den Kinderarzt: Grundzüge einer Biologie des Kindesalters. Edited by J. BROCK. Second edition, in two volumes. (Pp. xix+651 and xxxii+1183; illustrated. DM. 198.– for the two volumes.) Berlin: Springer-Verlag. 1954.

These two volumes are the second edition of a work, the first volume of the first edition having appeared more than 20 years ago. The increase in basic knowledge in this period of time has been so great that the second edition is virtually a new work, consisting of contributions by 26 authors.

The books are a remarkable assembly of biological and physiological facts concerning every aspect of the newborn and developing child, and there is a hint of the enormous difficulties which must have beset the editor of such a compendium in the fact that, while both volumes bear the date 1954, they were not received for review until November, 1955. The enormous worth of volumes such as these is clear to the most cursory inspection and the painstaking accuracy and minute detail with which the subject matter is handled are tributes to both authors and editor alike. Close inspection of the subject matter shows how wide-ranging is the information assembled and, indeed, it is difficult to think of anything concerning the being and development of the child which is not considered in detail.

Professor Brock is to be congratulated on his production. It is a pity that the work is in German, as otherwise it would cater for a far greater field. Perhaps Professor Brock and the publishers have considered the possibility of a translation into the English language—it would be assured of a warm welcome.

Die Papierchromatographie in der Kinderheilkunde. By H. BICKEL and F. SOUCHON; Foreword by Professor E. Rominger. (Pp. viii+151; 46 figures, 28 tables. DM. 27.–.) Stuttgart: Ferdinand Enke. 1955.

Anyone familiar with paediatric literature of recent years will know the name of Dr. Bickel in connexion with the application of paper chromatography to the metabolic problems of infancy and childhood. Dr. Bickel brings her experiences of Zurich and Birmingham and, most recently, Marburg, to those of Dr. Souchon's in Kiel and Bremen, and together they have written a monograph dealing exhaustively with their chosen subject.

There are sections on technical methods for the identification of amino-acids and sugars, and the normal physiological findings are considered in infancy and childhood. The bulk of the monograph, not unnaturally, considers the behaviour of the amino-acids in various diseases in which abnormal amino-acid patterns are expected or known. There is a short section on the different types of glycosuria and a special section on amino-acids in the duodenal juice by F. Wewalka.

A wealth of biochemical and clinical data is correlated factually and authoritatively, and to all those whose work is concerned with inborn errors of metabolism and the amino-acids this book can be recommended without hesitation. *Archiv fur Kinderheilkunde*, whose publication it is, are to be congratulated on their choice and the excellent production of their 31st supplement.

Rheumatoid Arthritis and Psoriasis Vulgaris. Internal and Cutaneous Manifestations of the Permanent Endoparasitism in the Homo Sapiens. Their Common Etiology, Pathogenesis, and Specific Vaccine Therapy. By TIBOR BENEDEK. (Pp. xii+308; illustrated. No price given.) Chicago: Dr. Tibor Benedek. 1955.

This is a remarkable 308-page monograph by Tibor Benedek, of Chicago, who is said on the title page to be Assistant Clinical Professor of Dermatology and Syphilology at the Stritch School of Medicine, and to be attending dermatologist at the Salvation Army Medical Centre in Chicago. The author states:

> 'During the last twenty-five years, by the use of adequate tools of research (bacteriology, immunology, histopathology) the writer has been able to show in a number of detailed publications that a group of the commonest skin diseases, *i.e.*, pompholyx, seborrhoeic dermatitis, psoriasis vulgaris, pityriasis rosea and hidradenitis suppurativa, are cutaneous reactions to a single causative bacterial agent, the permanent endoparasite o- the human race, the *B. endoparasiticus Benedek* 1927.'

The organism, he says, is also the cause of rheumatoid arthritis. In his introduction he castigates dermatologists, rheumatologists, bacteriologists and other research workers for their obtuseness in not making this discovery and for their insufficient knowledge of the great achievements of investigators of past decades. In this respect he refers in part to the pioneering work of Gilbert Bannatyne, one time consulting physician of the Royal Mineral Water Hospital, Bath, England, for his outstanding contributions in obtaining the first blood culture of dumb-bell shaped bacilli from cases of rheumatoid arthritis identical with those which he found in synovial and joint connective tissues.

He claims that the organism can be repeatedly recovered from cantharides blisters, and says that the only treatment of value is a vaccine made from his organism. He discusses a specific allergic skin test with the vaccine, but remarks that no control cases are possible, because every human being is allergic to his own endoparasite, and every human being has this endoparasite within him.

The occasional ameliorating effect of pregnancy is explained by the fact that the foetal endoparasite enters the maternal circulation and most probably acts like an intravenous vaccine perfusion during the whole of pregnancy, causing the desensitization of the allergic synovial and articular tissues.

Comment is superfluous.